

VA National Center for PTSD

PTSD Consultation Program Webinar

November 20, 2019

Addressing Sleep: A Strategy for Symptom Reduction & Suicide Prevention

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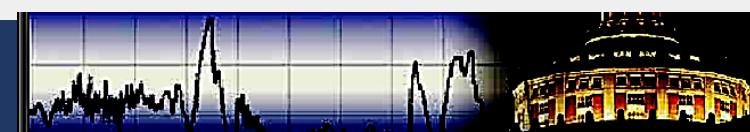
- National Institutes of Health: R01 NR013909; R01 CA175053; R21 AG041942; K23 NR010408; F32 NS049789; R21 AG023956; L30 MH087269
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Disclaimer:

The views or opinions expressed in this talk do not represent those of the Department of Veterans Affairs or the United States Government.



URMC Sleep & Neuro- Physiology Research Lab



VA Ctr of Excellence for Suicide Prevention



An Outline in Four Premises

1. **Sleep Disturbance (e.g., *insomnia*) exacerbates and causes medical and psychiatric morbidity**

The image shows a screenshot of the CDC's website. At the top left is the CDC logo with the text "Centers for Disease Control and Prevention" and "CDC 24/7: Saving Lives, Protecting People™". Below the logo is the title "Insufficient Sleep Is a Public Health Problem". To the right of the title are social media icons for Facebook, Twitter, and a plus sign, followed by a language selection box set to "English". A large blue header box contains the text "Poor Sleep/Sleep Duration associated with:" followed by a bulleted list of health issues.

Poor Sleep/Sleep Duration
associated with:

- *All-cause mortality*
- *Metabolic syndrome*
- *Diabetes/glucose control*
- *Hypertension*
- *Coronary heart disease*
- *Depression*
- *Neurobehavioral performance decrements*

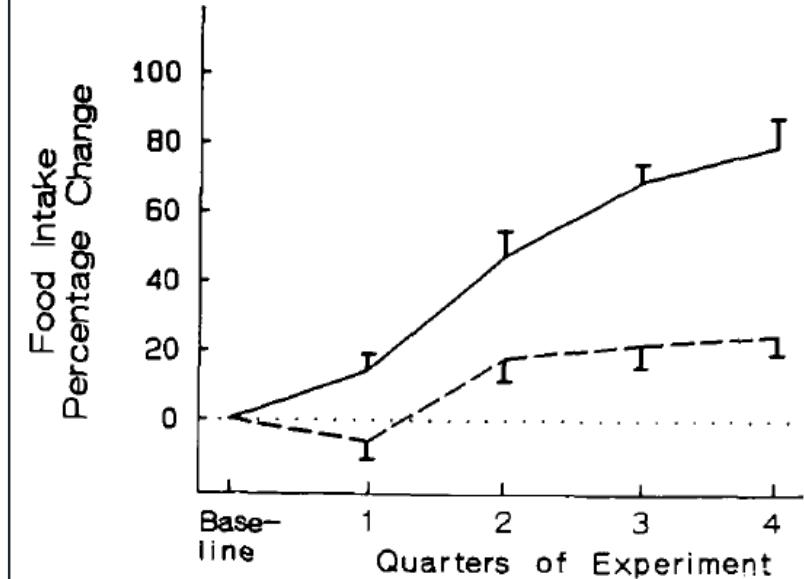
An Outline in Four Premises

1. Sleep Disturbance (e.g., *insomnia*) exacerbates and causes medical and psychiatric morbidity

Sleep Deprivation in the Rat:

Emerson, Bergmann & Rechtshaffan, SLEEP, 12(1) 1989

Totally sleep deprived rats died within 11-32 days ...with lesions & weight loss despite higher caloric intake than yoked controls that remained healthy.



An Outline in Four Premises

1. Sleep Disturbance (*e.g., insomnia*) exacerbates and causes medical and psychiatric morbidity
2. **The efficacy, effectiveness and limited AE profile of *Cognitive Behavioral Therapy for Insomnia (CBT-I)* 'should' make Rx of hypnotics rare**

Management of Chronic Insomnia Disorder in Adults: A Clinical Practice Guideline From the American College of Physicians

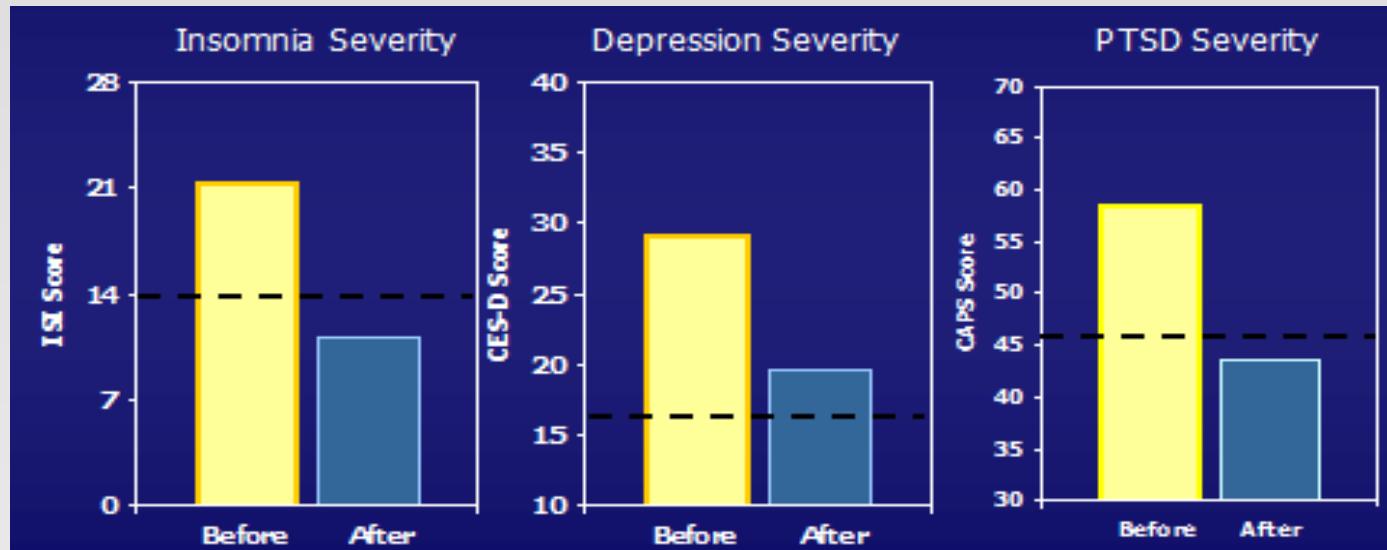
Recommendation 1: All adult patients receive CBT-I as the initial treatment for chronic insomnia disorder.

Recommendation 2: Clinicians use a shared decision-making approach, including a discussion of the benefits, harms, and costs of short-term use of medications, to decide whether to add pharmacological therapy in adults with chronic insomnia disorder in whom CBT-I alone was unsuccessful.

An Outline in Four Premises

1. Sleep Disturbance (*e.g., insomnia*) exacerbates and causes medical and psychiatric morbidity
2. The efficacy, effectiveness and limited AE profile of CBT-I ‘should’ make Rx of hypnotics rare
3. **Treating insomnia improves more than sleep**

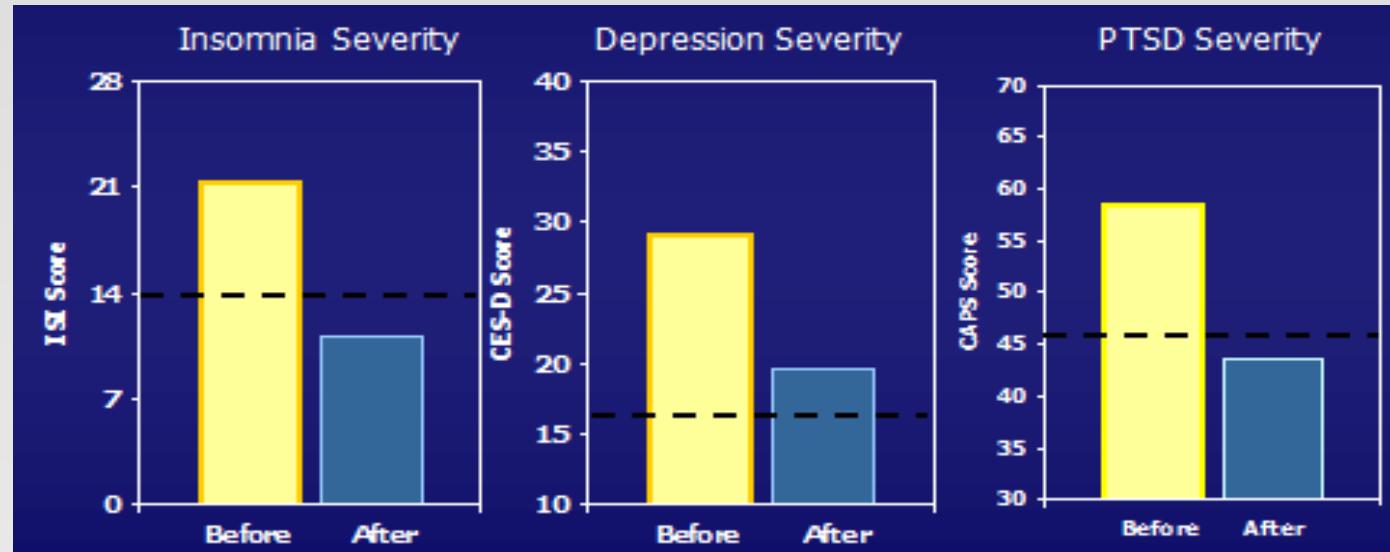
Single Arm 8-Session CBT-I for Combat Veterans (N=15)



An Outline in Four Premises

1. Sleep Disturbance (*e.g., insomnia*) exacerbates and causes medical and psychiatric morbidity
2. The efficacy, effectiveness and limited AE profile of CBT-I ‘should’ make Rx of hypnotics rare
3. Treating insomnia improves more than sleep
4. **CBT-I is an anti-depressant with suicide preventing side effects**

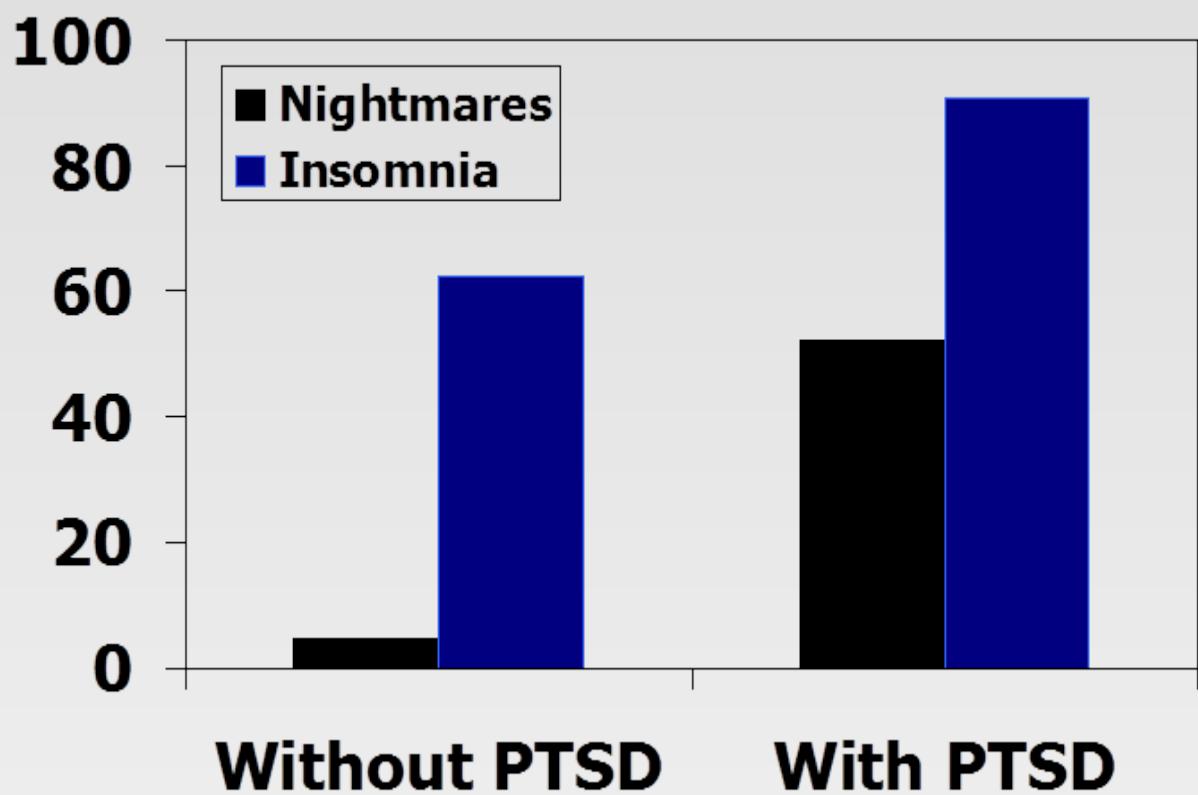
Single Arm 8-Session CBT-I for Combat Veterans (N=15)



3 Subjects endorsing Suicidality at baseline
None at post-treatment.

1. Insomnia & Morbidity: (a) PTSD

Prevalence (%) of Nightmares & Insomnia among Vietnam Era Combat Veterans



- Disrupted sleep mediates relationship between PTSD and medical morbidity
- Nightmares respond to PTSD Tx; Insomnia, not so much.
- The presence of insomnia reduces PTSD remission rates

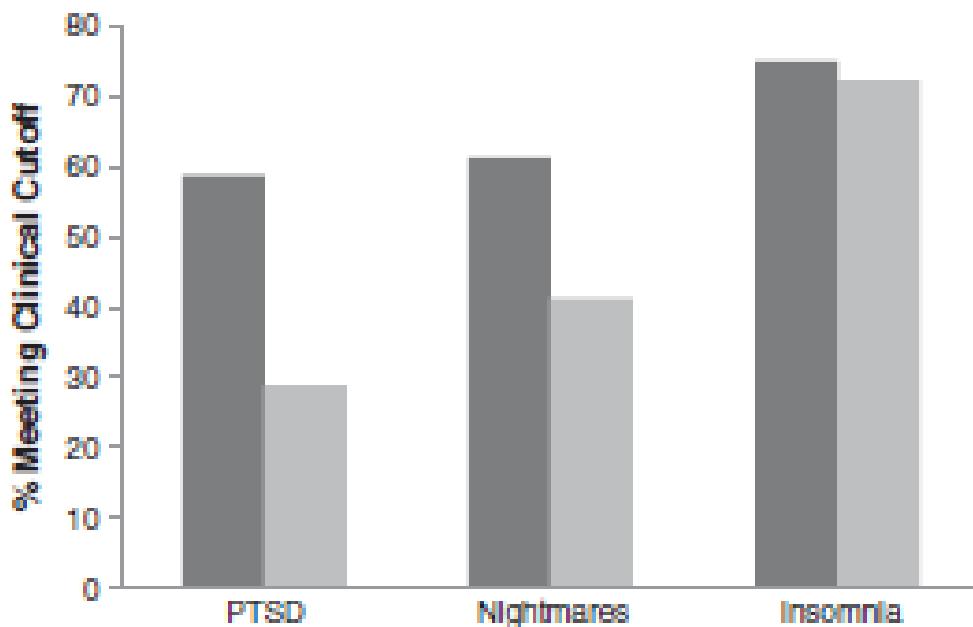
Clum, Nishith & Resick, J Nerv Mental Dis. 2001;189:618-22

Gutner et al., Behav Res Ther 2013;51:817-22.

Marcks, et al., Psychiatry Res. 2010;178:487-92.

1. Insomnia & Morbidity: (a) PTSD

6-Month Observational Study of Iraq/Afghanistan Veterans (N=72)



- Insomnia predicts 6 Mo PTSD severity (ANCOVA; $p=.005$)
- Baseline insomnia associated with higher rate of PTSD (38%) vs, No insomnia (5%)

- Disrupted sleep mediates relationship between PTSD and medical morbidity
- Nightmares respond to PTSD Tx; Insomnia, not so much.
- The presence of insomnia reduces PTSD remission rates

Clum, Nishith & Resick, J Nerv Mental Dis. 2001;189:618-22

Gutner et al., Behav Res Ther 2013;51:817-22.

Marcks, et al., Psychiatry Res. 2010;178:487-92.

1. Insomnia & Morbidity: (b) Depression



Pergamon

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SLEEP DISORDERS AND DEPRESSION: THE 'CHICKEN AND EGG' SITUATION

MYRIAM M. M. P. VAN MOFFAERT

FROM THE BENCH TO THE BEDSIDE

Insomnia and Depression: If it Looks and Walks Like a Duck...

Comment on Taylor DJ, Lichstein KL, Durrence HH, et al. Epidemiology of insomnia, depression, and anxiety. *SLEEP* 2005; 28(11): 1457-1464.

Fred W. Turek, PhD

Center for Sleep and Circadian Biology, Northwestern University, Evanston, IL

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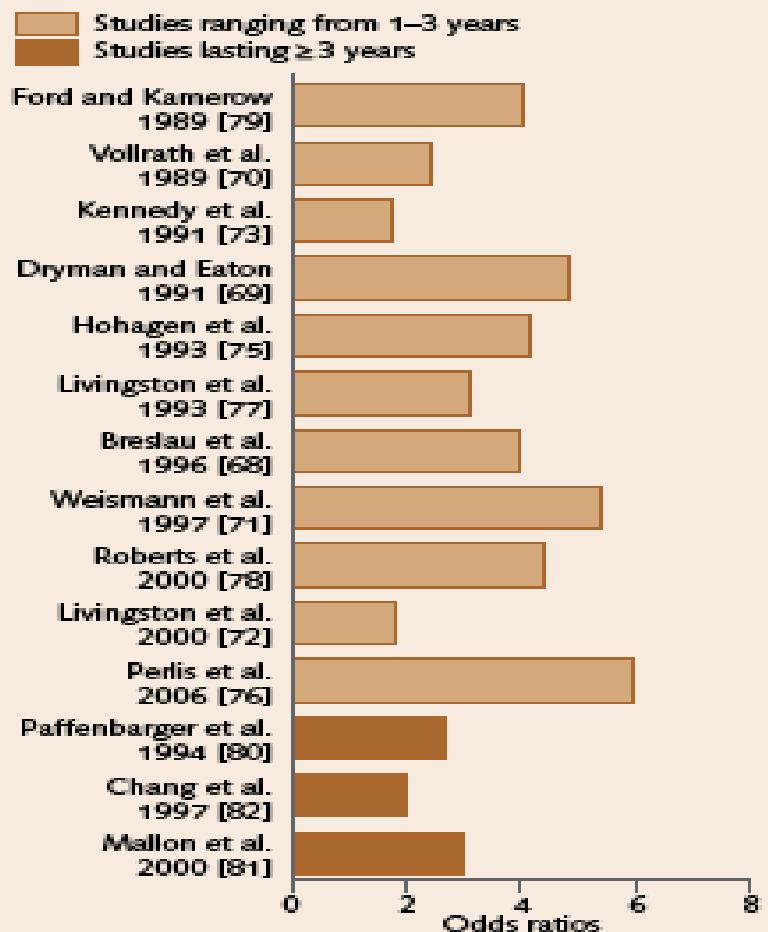
Insomnia and Depression: Birds of a Feather?

Wilfred R Pigeon and Michael L Perlis

Sleep and Neurophysiology Research Laboratory, University of Rochester, Rochester, NY, USA

Over the course of the last 30 years there has been a great deal of research into sleep abnormalities in patients with major depression. However, only a small proportion of this work has focused on sleep continuity disturbance (as opposed to abnormalities in sleep micro- and macroarchitecture), despite insomnia being a defining feature of depression. The lack of work in this area may be attributed to the view that insomnia is nothing more than a symptom of depression. Yet, in recent years, perceptions have shifted to the alternative point of view – that insomnia is less a symptom and more a comorbid disorder. The present article provides an overview of the data and suggests that insomnia and depression are separable entities, insomnia confers a risk for greater depressive morbidity, and targeted treatment for insomnia may influence the clinical course of major depression. *Int J Sleep Disorders* 2007;1(3):82-91.

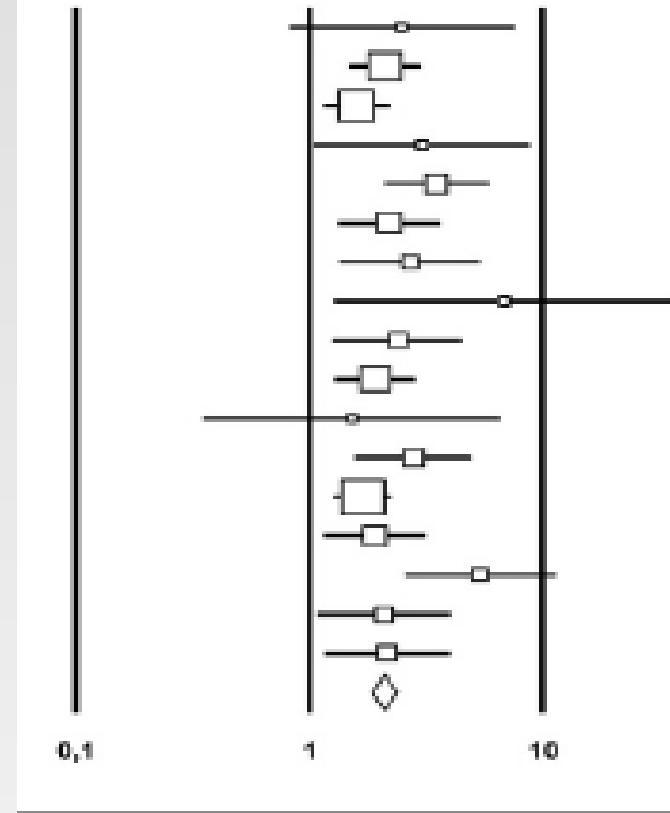
Figure 2. Odds ratios from longitudinal studies showing the elevated risk for the development or presence of depression when there are symptoms of sleep disturbance consistent with persistent insomnia.



Incidence of Subsequent Depression

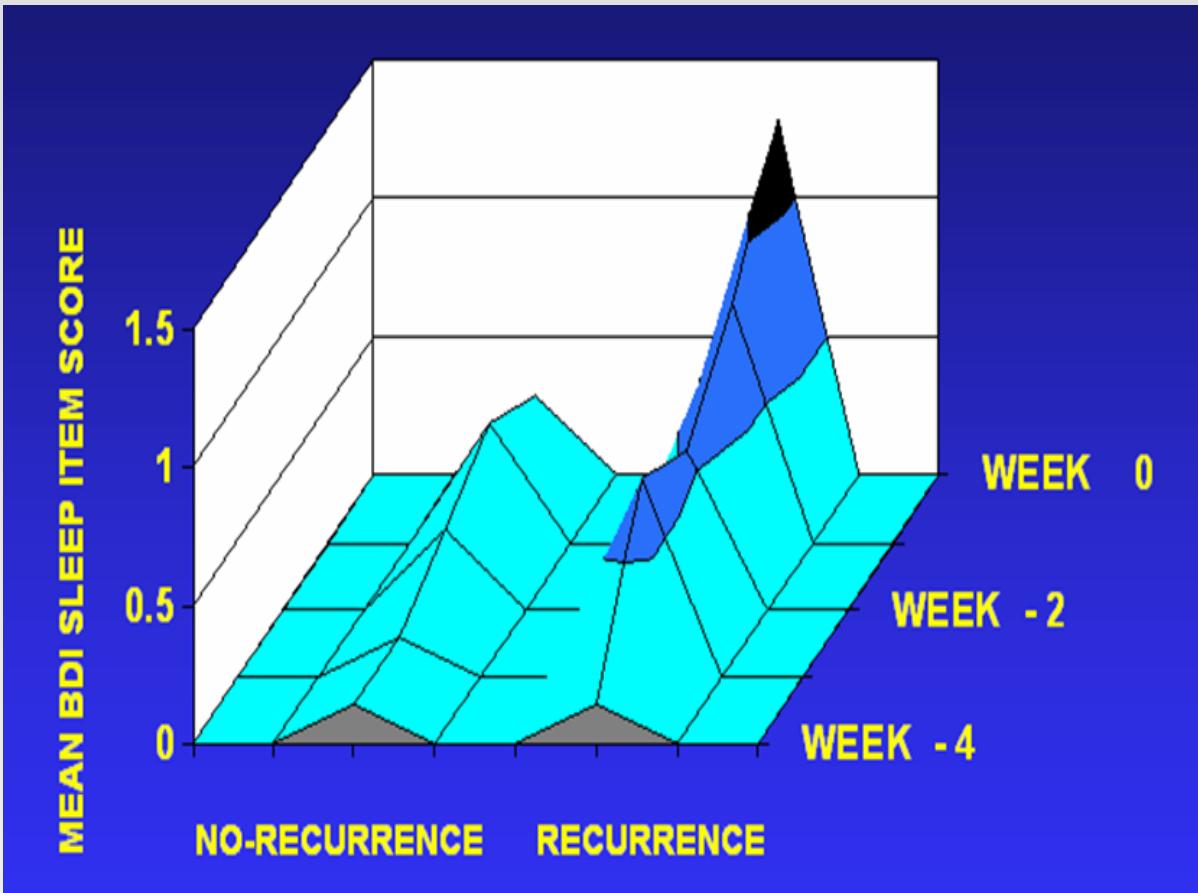
No Insomnia	4.0%
Baseline Insomnia	13.1%

$$OR = 2.1 [95\% CI: 1.9-2.4]$$



1. Insomnia & Morbidity: (b) Depression

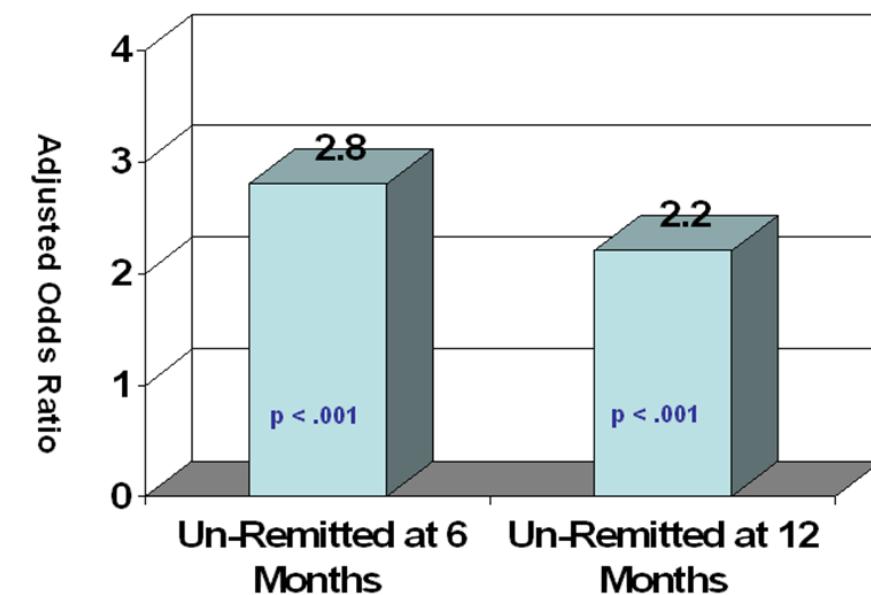
Insomnia as Prodrome to MDD Episodes



Perlis et al., *J Affective Disorders*, 1997

Insomnia blunts Depression Tx Response

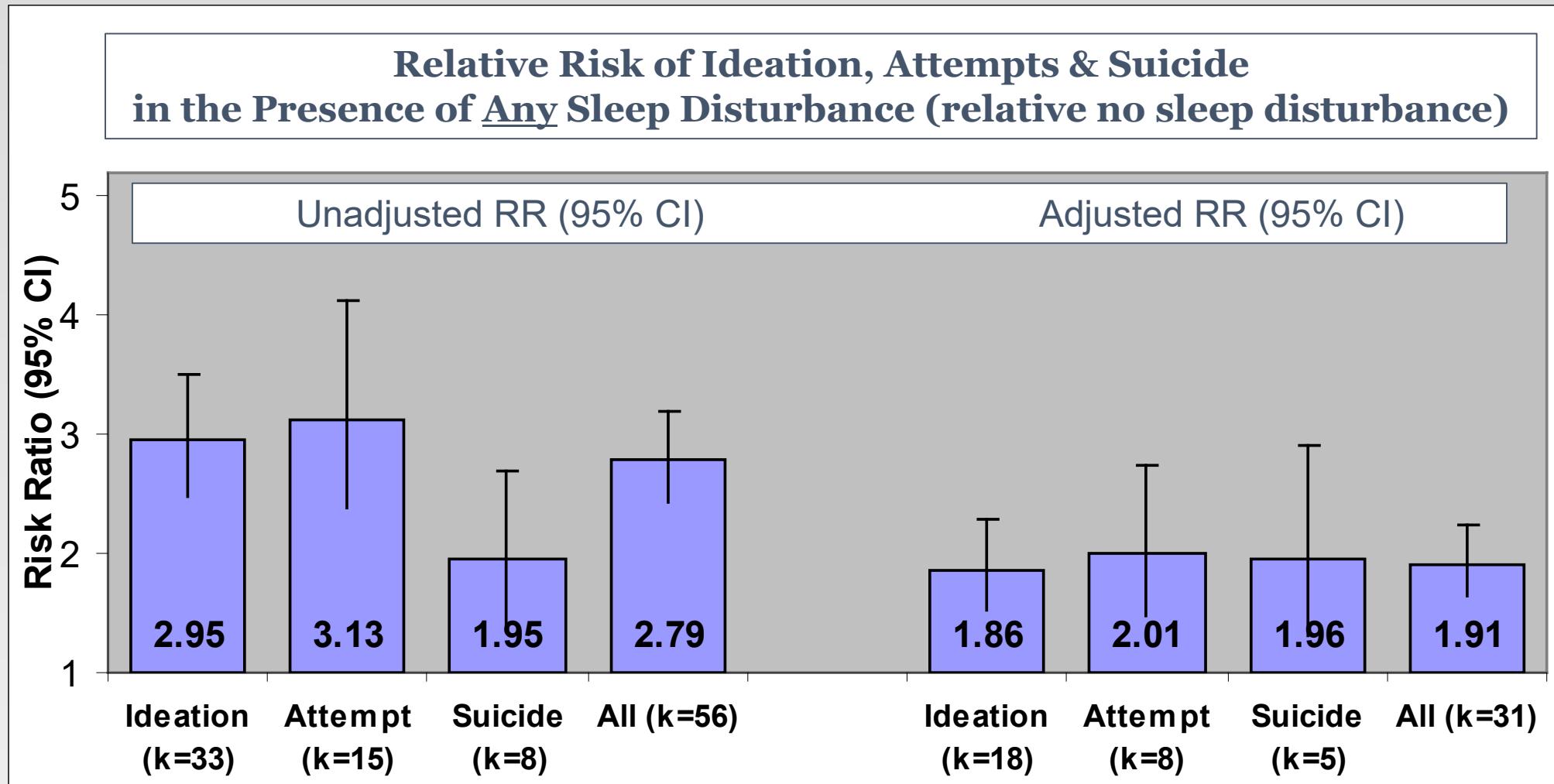
Adjusted Odds Ratios of Remaining Depressed (SCID MDD)
for Persistent Insomnia Compared to No Insomnia



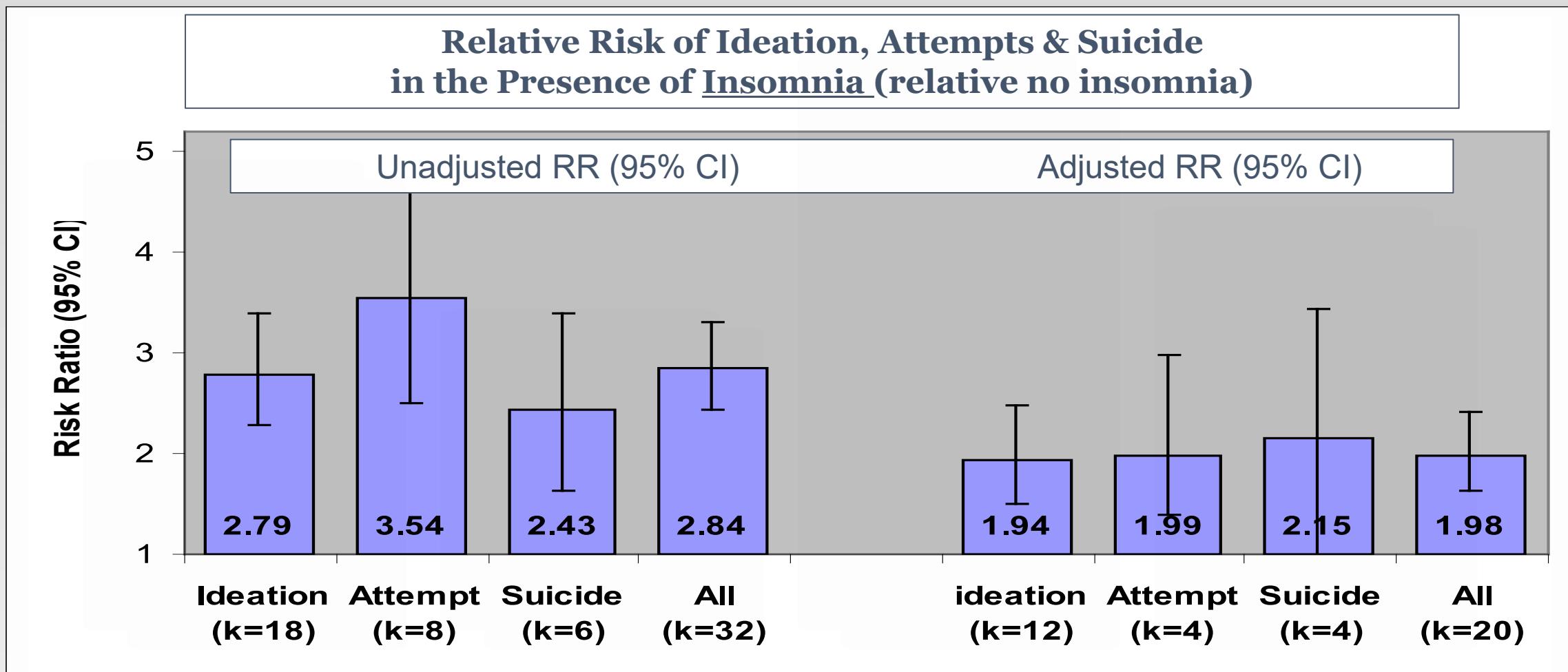
Odds ratios adjusted for intervention arm, baseline depression severity and number of chronic illnesses.

Pigeon, Hegel, et al. *Sleep*, 2008, 31(4).

1. Insomnia & Morbidity: (c) Suicide

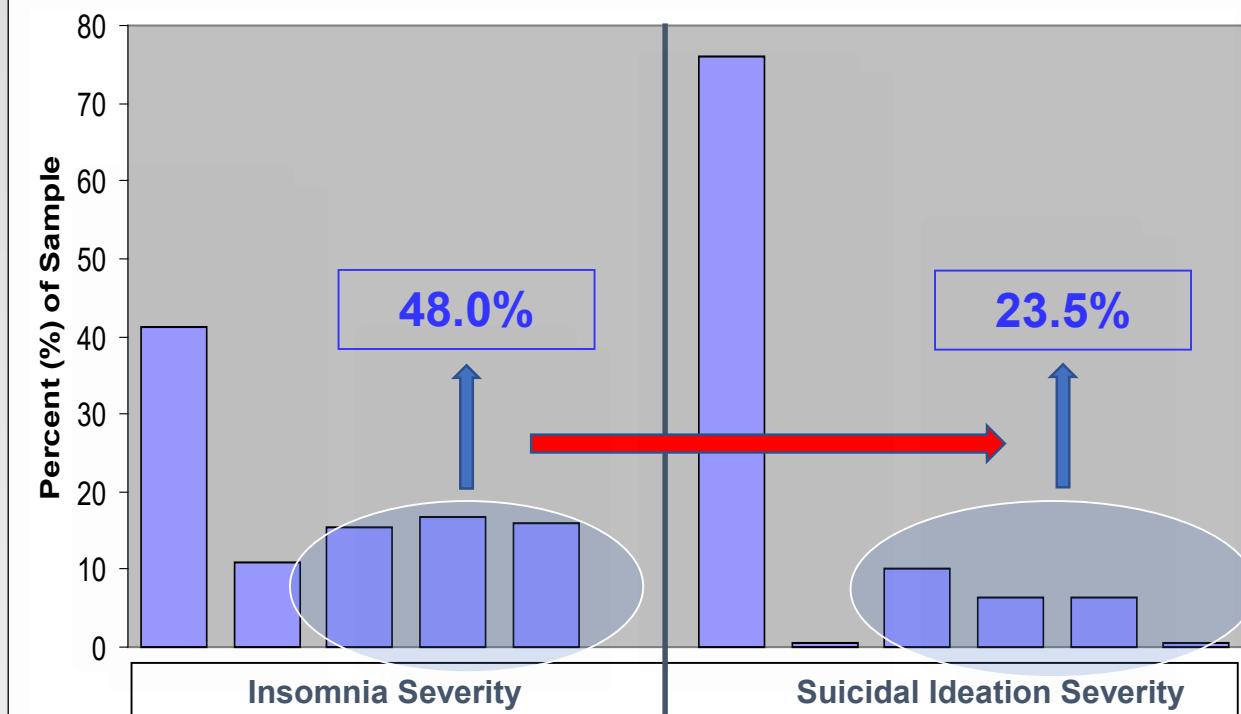


1. Insomnia & Morbidity: (c) Suicide



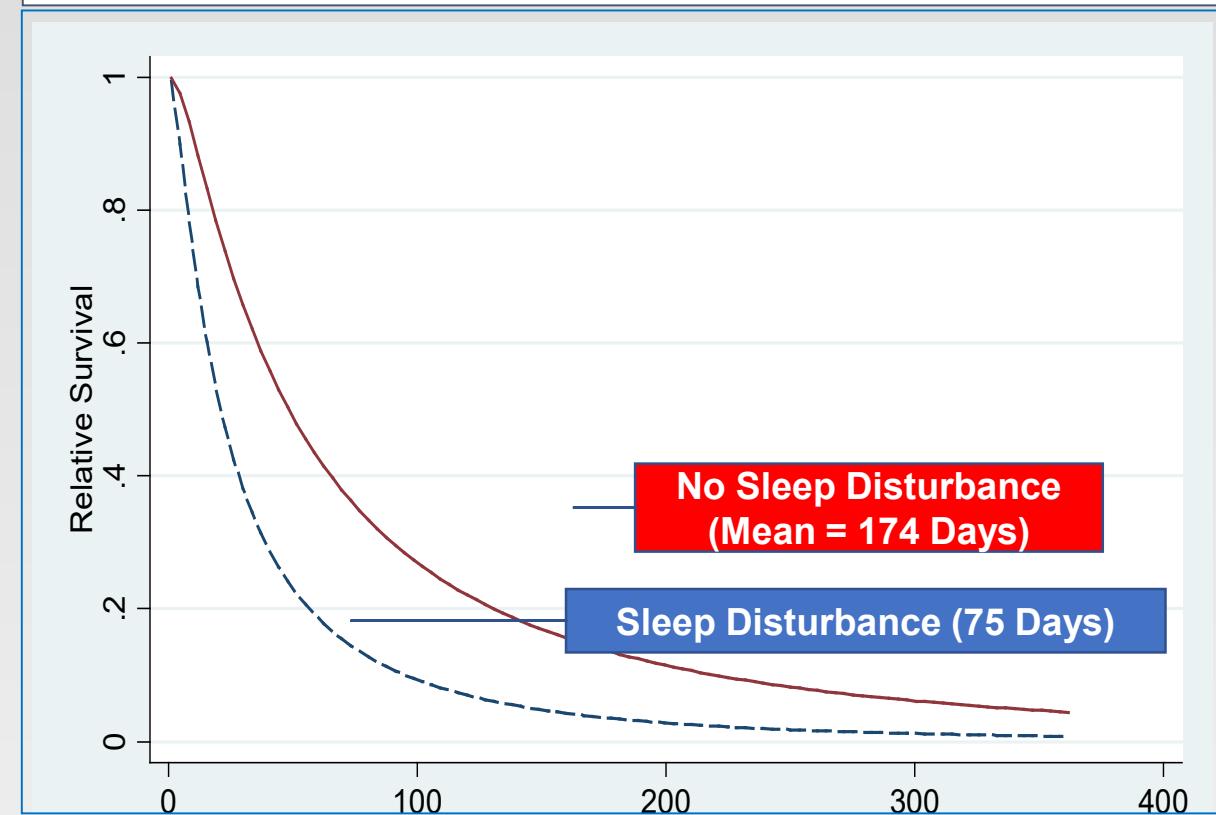
1. Insomnia & Morbidity: (c) Suicide

Insomnia & Ideation among Veterans referred to Behavioral Telehealth (N=654)



Multiple Regression analysis controlling for age,
gender, etoh, depression **p < .01**

Time to Death among Veteran Suicide Decedents (N=381)



Premise 2: Why CBT-I and Not Sedative-Hypnotics

1. CPGs, meta-analyses, comparative meta-analyses & head-to-head trials

- Smith, et al. Comparative meta-analysis of pharmacotherapy and behavior therapy for persistent insomnia. *Am J Psychiatry* 2002;159(1):5-11.
- Mitchell, et al. Comparative effectiveness of cognitive behavioral therapy for insomnia: a systematic review. *BMC Fam Prac*
- Hofmann, et al. The efficacy of cognitive behavioral therapy: A Review of meta-analyses. *Cognit Ther Res* 2012;36(5):427-440.

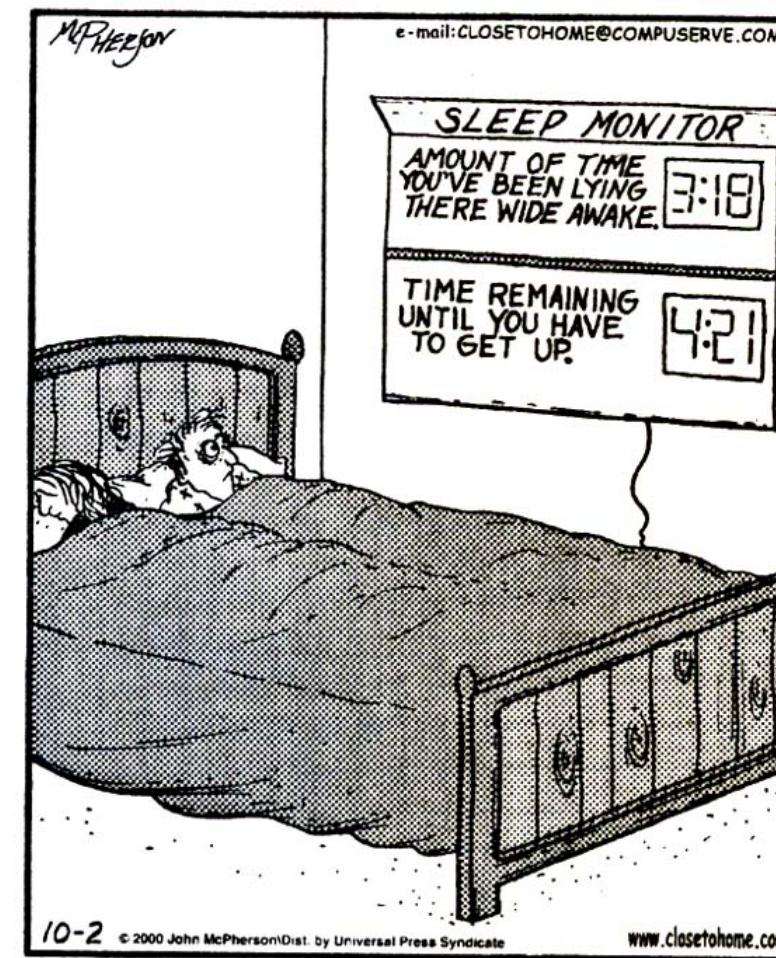
Premise 2: Why CBT-I and Not Sedative-Hypnotics

1. CPGs, meta-analyses, comparative meta-analyses & head-to-head trials
2. Humans engage in sleep-interfering behaviors and cognitions

**“Sleep is the most moronic fraternity
in the world, with the heaviest dues
and the crudest rituals.”**

---Vladimir Nabokov

CLOSE TO HOME JOHN MCPHERSON



Premise 2: Why CBT-I and Not Sedative-Hypnotics

1. CPGs, meta-analyses, comparative meta-analyses & head-to-head trials
2. Humans engage in sleep-interfering behaviors and cognitions
3. **Limited adverse events**

Clinical Practice Guideline for the Pharmacologic Treatment of Chronic Insomnia in Adults: An American Academy of Sleep Medicine Clinical Practice Guideline

Michael J. Sateia, MD¹; Daniel J. Buysse, MD²; Andrew D. Krystal, MD, MS³; David N. Neubauer, MD⁴; Jonathan L. Heald, MA⁵

“We suggest that clinicians not use trazodone as a treatment for sleep onset or sleep maintenance insomnia (vs. no treatment) in adults.”

“Harm outweighs benefits.”

Premise 2: Why CBT-I and Not Sedative-Hypnotics

1. CPGs, meta-analyses, comparative meta-analyses & head-to-head trials
2. Humans engage in sleep-interfering behaviors and cognitions
3. **Limited adverse events**

Table 6: Adjusted Incidence of Suicide Attempts by Index Prescription: Zolpidem versus Trazodone

Agents	N	Suicide Attempts per 100,000 person yrs	Adjusted HR Suicide Attempt (95% CI)
COX PROPORTIONAL HAZARD MODEL 1			
Trazodone	76,215	76.3	1.61 (1.07-2.43)
Zolpidem	76,215	50.9	

Premise 2: Why CBT-I and Not Sedative-Hypnotics

1. CPGs, meta-analyses, comparative meta-analyses & head-to-head trials
2. Humans engage in sleep-interfering behaviors and cognitions
3. Limited adverse events
4. **Wide effectiveness**

CBT-I efficacy has been demonstrated in a wide range of populations including in patients with:

- Depression, Anxiety & PTSD
- Chronic Pain
- Cancer (post-chemo/radiation therapy)
- Bipolar Disorder
- Delusions & Hallucinations

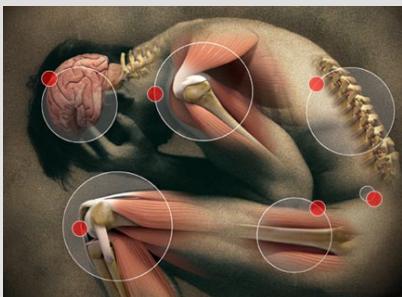
Premise 2: Why CBT-I and Not Sedative-Hypnotics

1. CPGs, meta-analyses, comparative meta-analyses & head-to-head trials
2. Humans engage in sleep-interfering behaviors and cognitions
3. Adverse events
4. Wide effectiveness
5. **You can do it here or there**



Premise 3: Treating insomnia improves more than sleep

A. In Patients with Chronic Pain



Adults with Chronic Neck or Back Pain

Baseline Assessments
Self-report battery
Screening Polysomnography

Randomization (N=28 @ 2:1)

8 wk CBT-I
(n = 19)

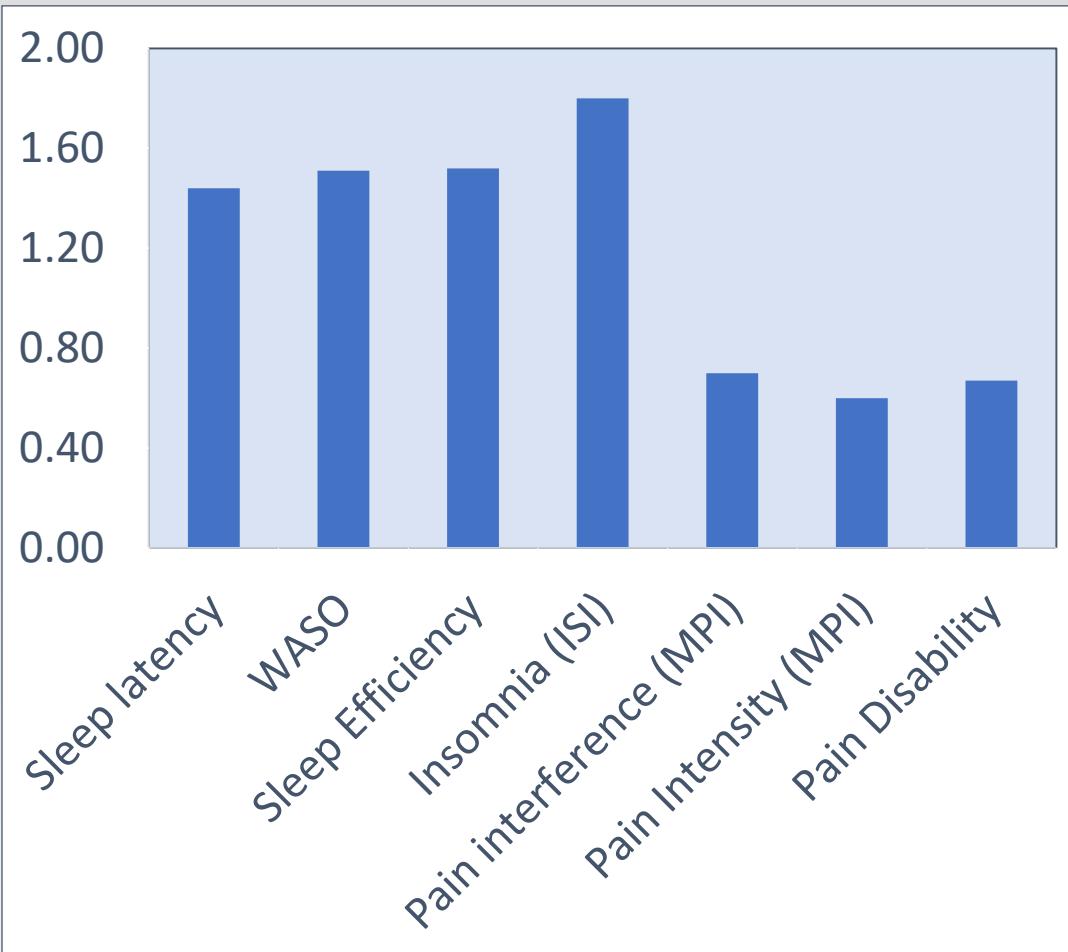
Attention CTRL
(n = 9)

Post-Tx, 3 Mo & 6 Mo Assessments

NIH Support: R21 NR009080

3: CBT-I improves more than sleep: (a) Pain-1

Effect Sizes (Hedges g): CBT-I vs. CTRL



Adults with Chronic Neck or Back Pain

Baseline Assessments
Self-report battery
Screening Polysomnography

Randomization (N=28 @ 2:1)

8 wk CBT-I
(n = 19)

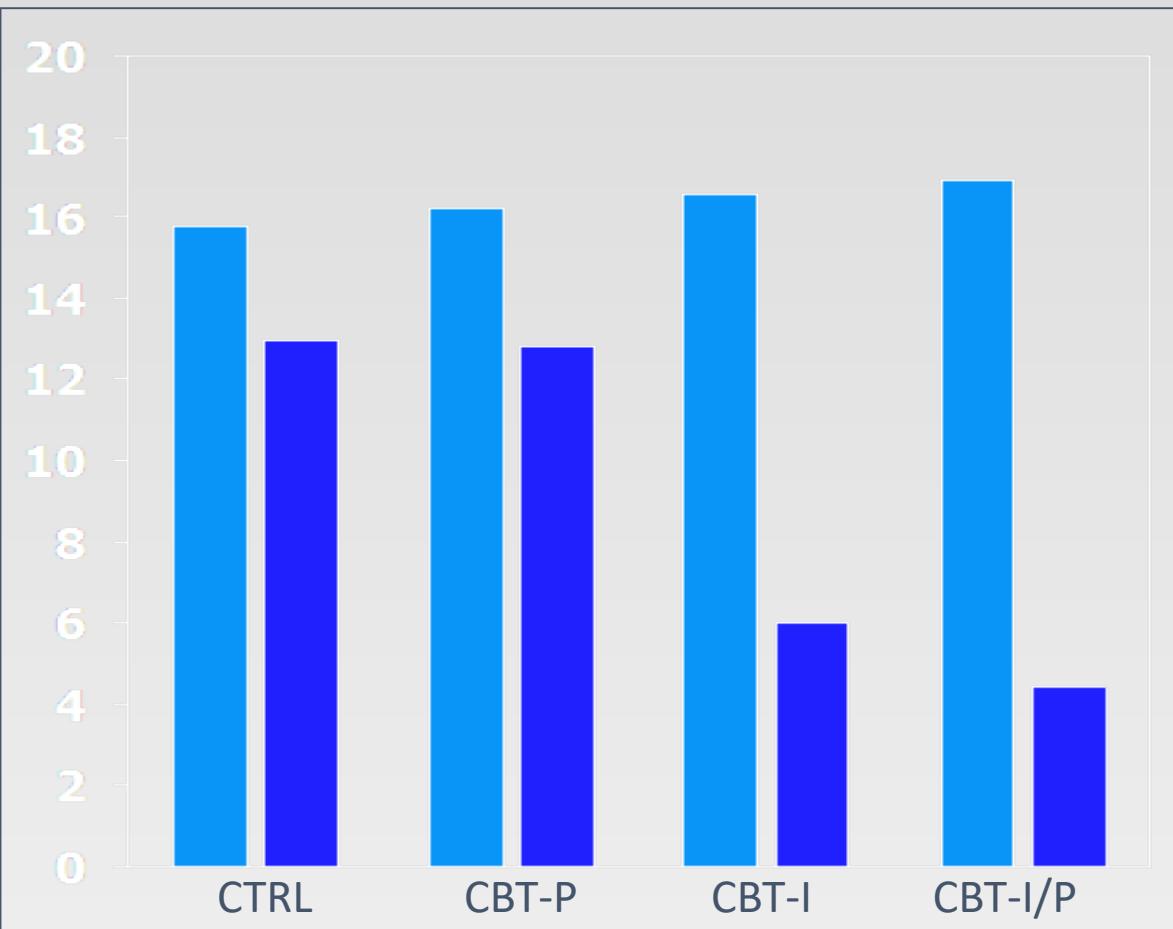
Attention CTRL
(n = 9)

Post-Tx, 3 Mo & 6 Mo Assessments

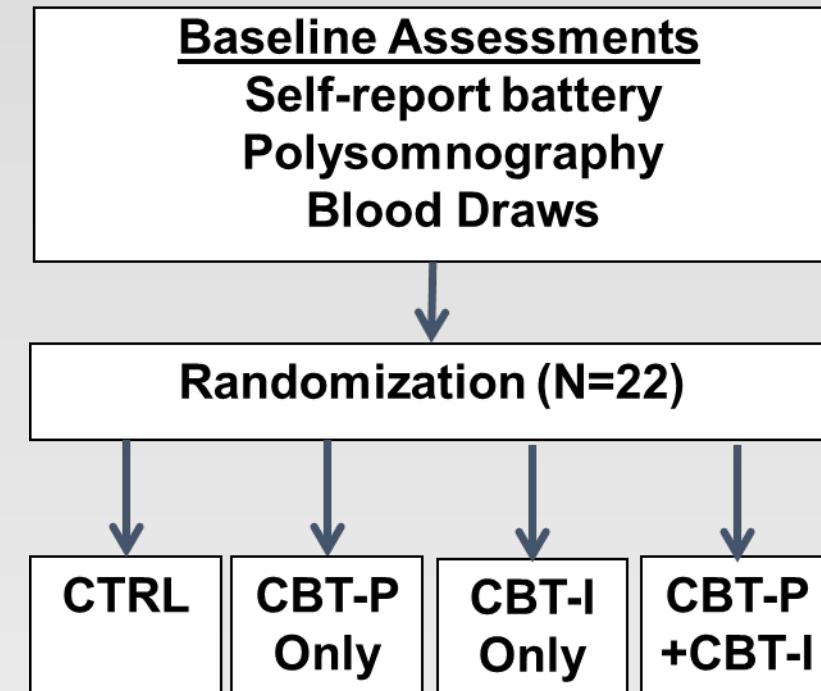
NIH Support: R21 NR009080

3: CBT-I improves more than sleep: (a) Pain-2

Insomnia Severity Pre-Post



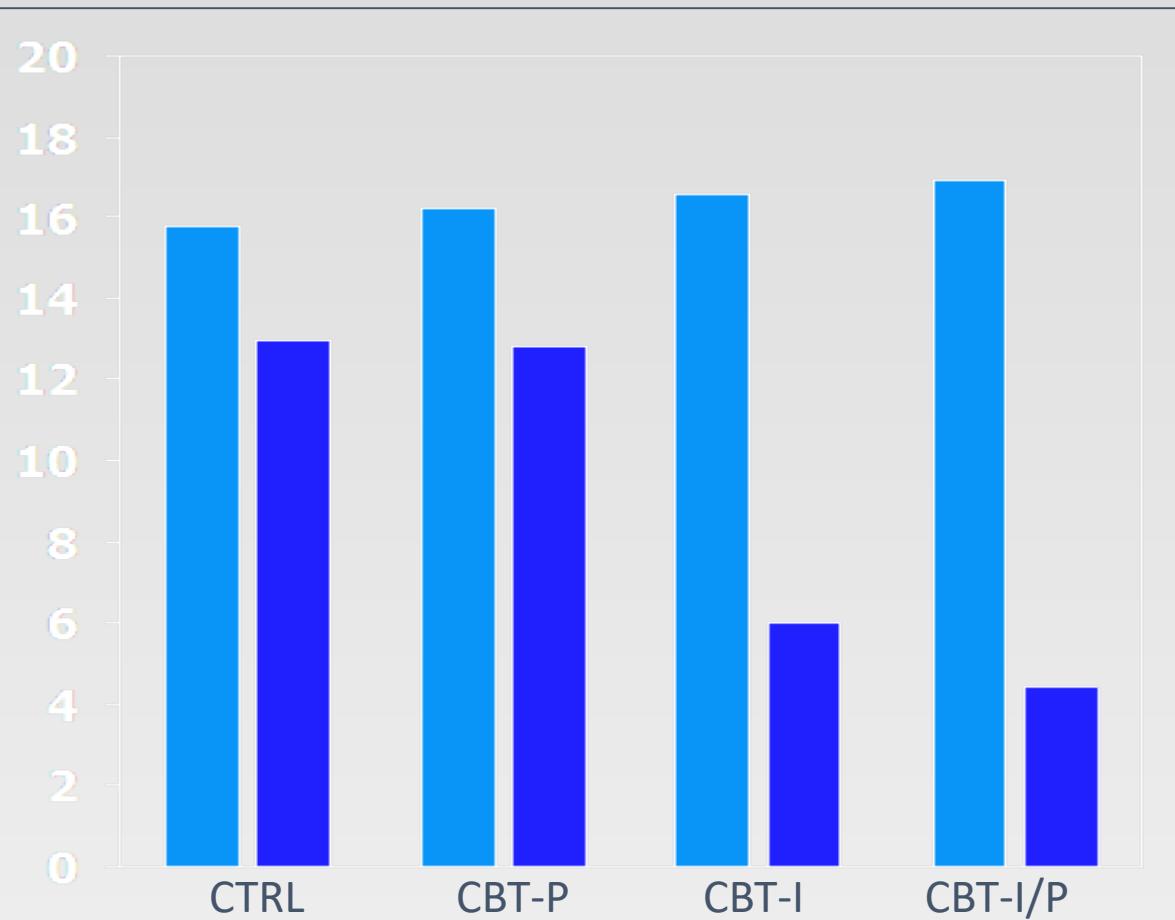
Adults with Chronic Neck or Back Pain



NIH Support: F32 NS049789

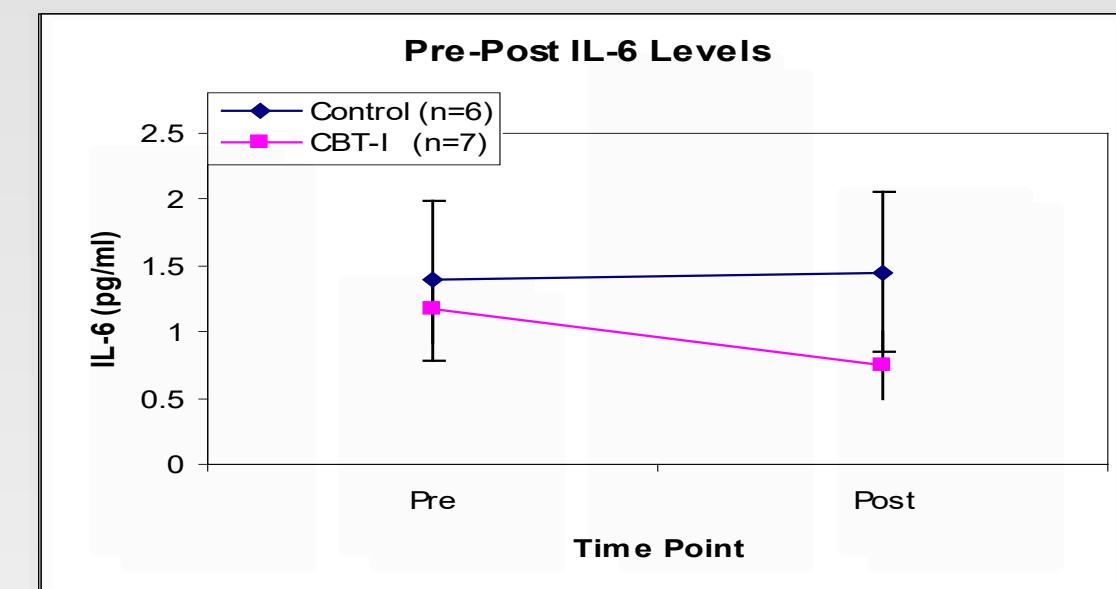
3: CBT-I improves more than sleep: (a) Pain-2

Insomnia Severity Pre-Post



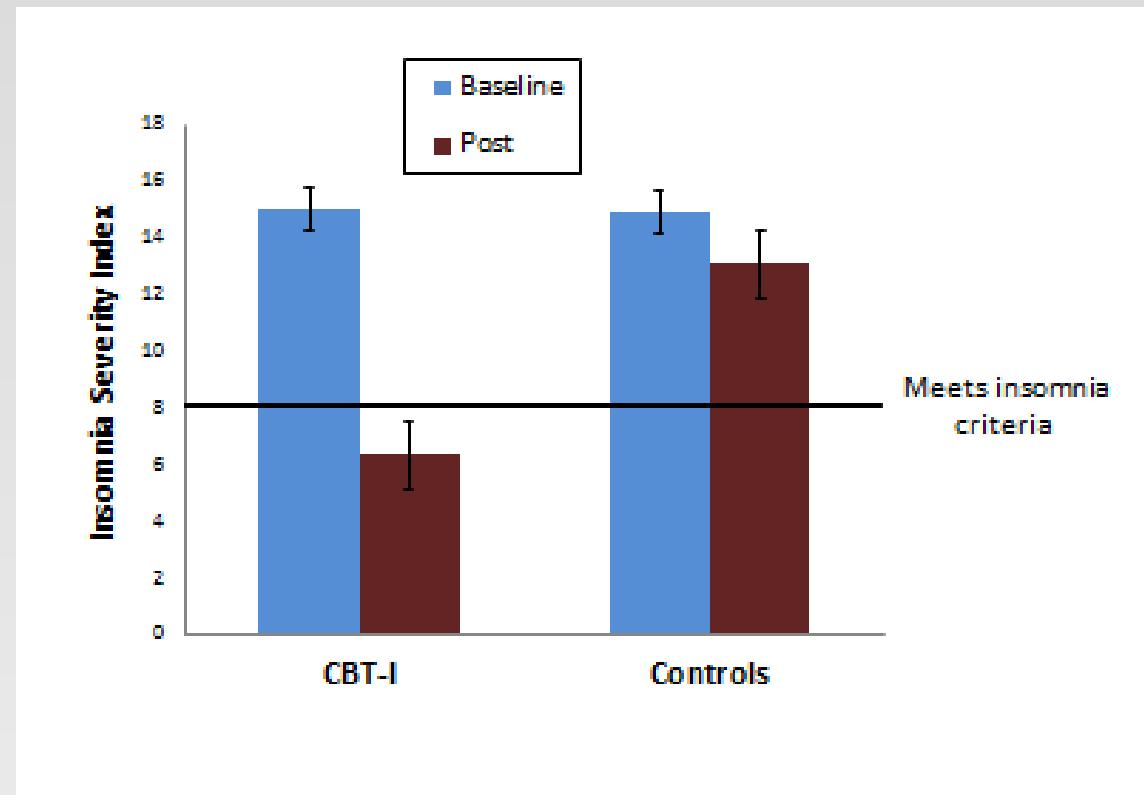
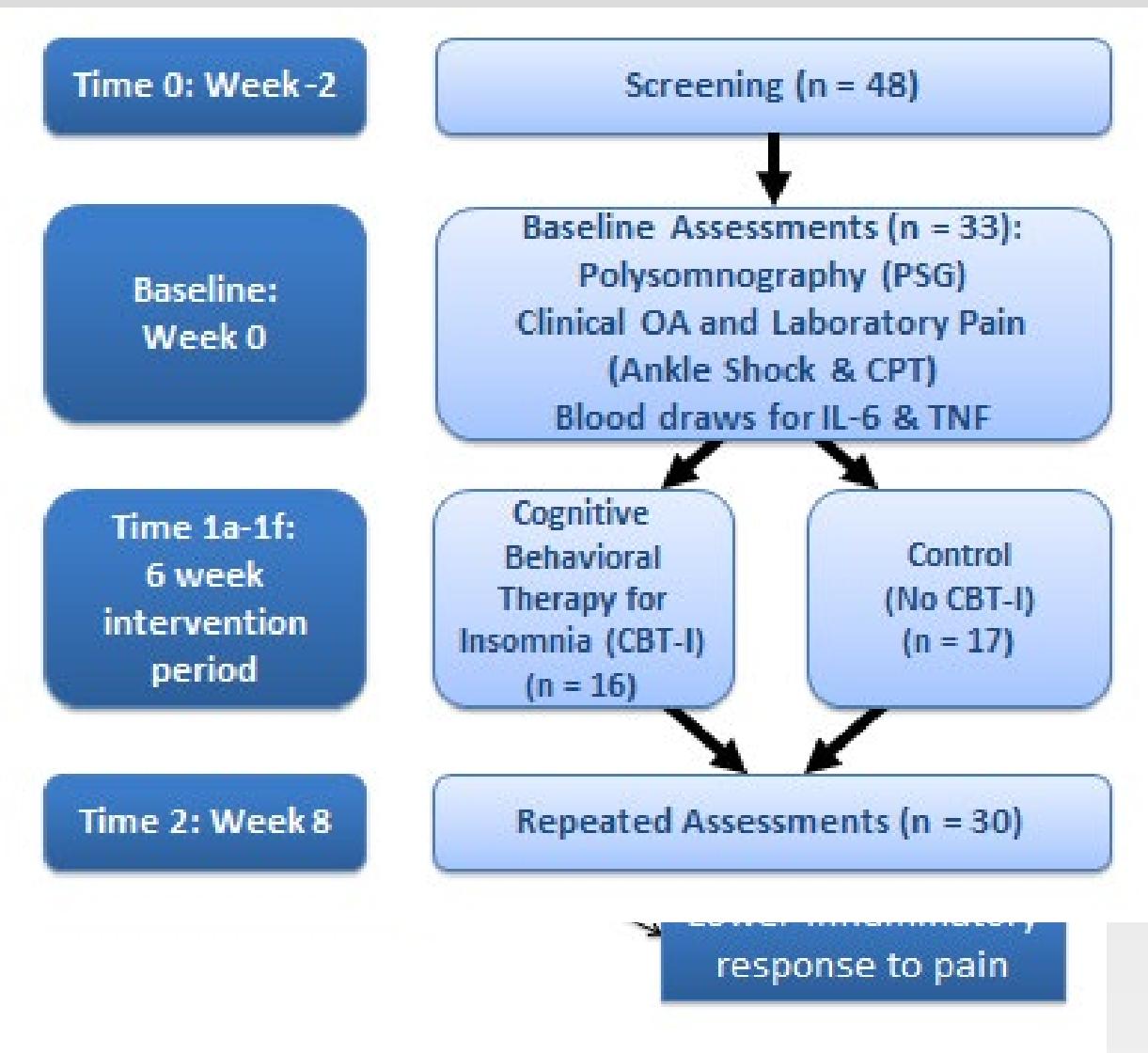
Effect Sizes (Hedges g): CBT-I vs. CTRL

Insomnia Severity	1.64
Pain Disability	0.27
Depression	3.86
Fatigue	0.78



NIH Support: F32 NS049789

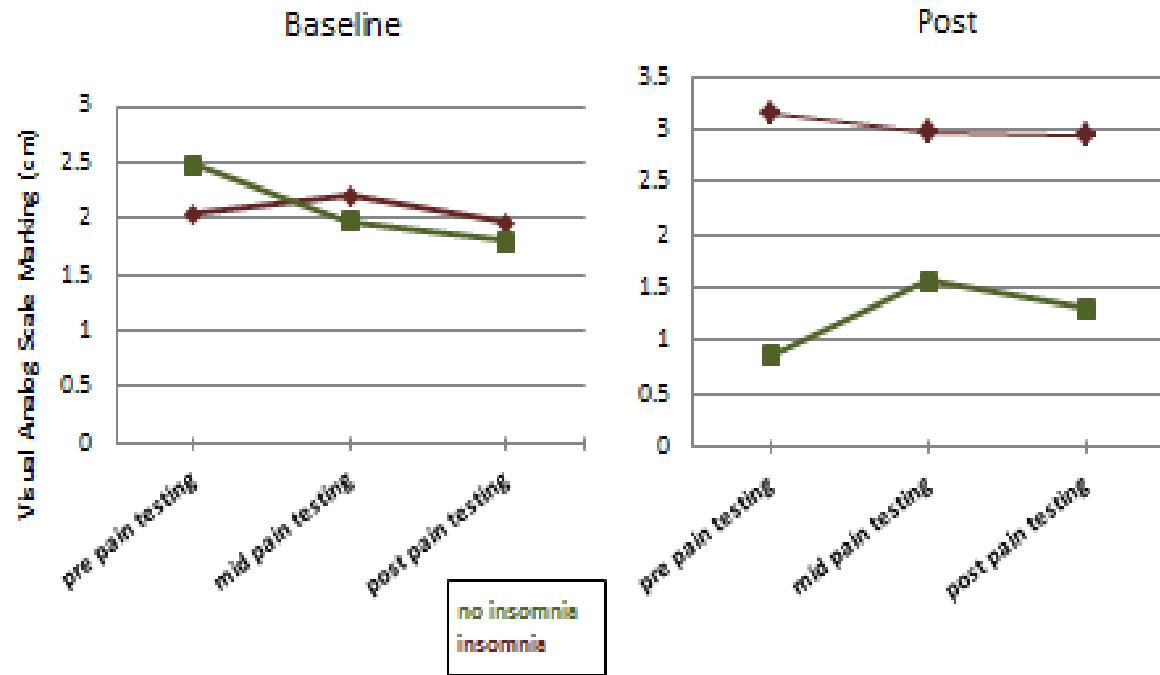
3: CBT-I improves more than sleep: (a) Pain-3



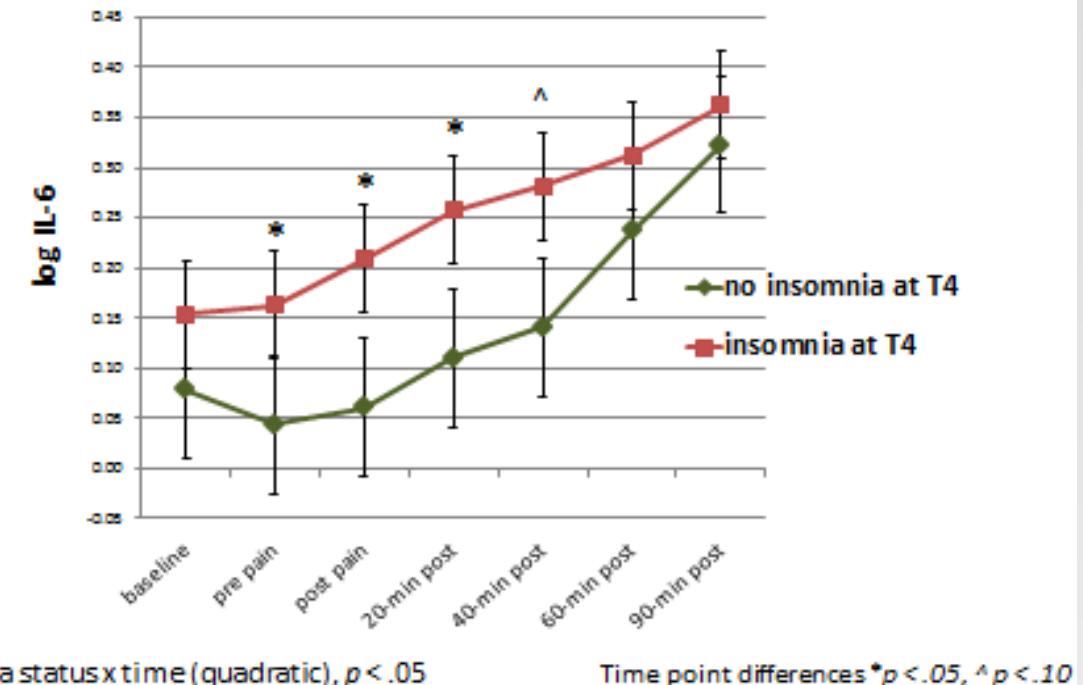
NIH Support: R21 AG041942

3: CBT-I improves more than sleep: (a) Pain-3

Reduced Pain during the Pain Testing Session



Lower IL-6 Response Across Pain Testing



NIH Support: R21 AG041942

3: CBT-I improves more than sleep: (b) PTSD/MDD

- A. In Patients with Chronic Pain
- B. In Patients with PTSD & MDD

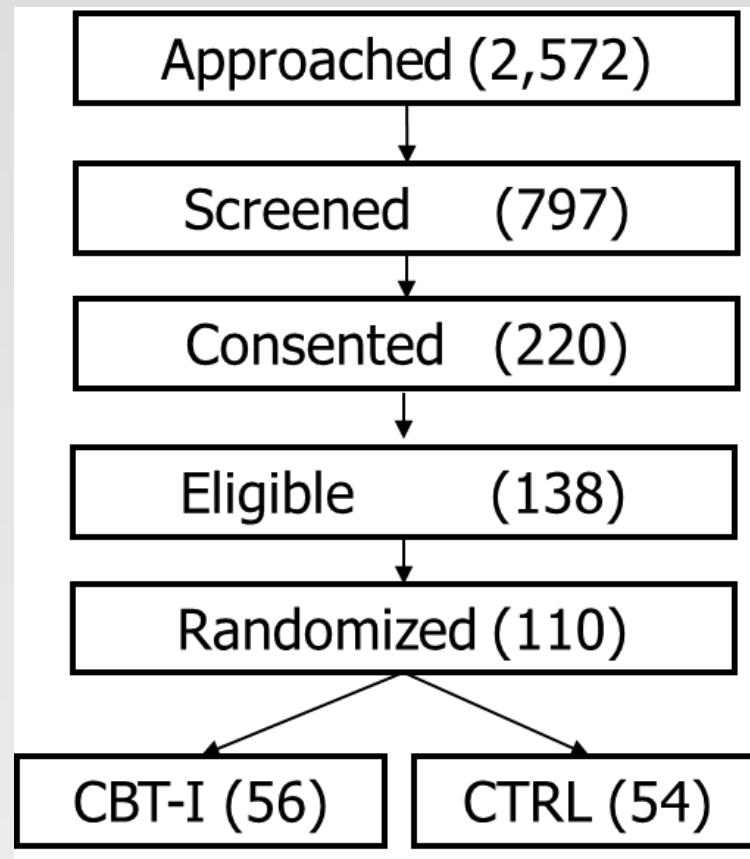
A Randomized Clinical Trial of CBT-I
for Survivors of Interpersonal Violence

Inclusion: Exposure to IPV in past yr;
+ PTSD + MDD + Insomnia

1. Will CBT-I improve insomnia, PTSD and depression Sxs ?
2. Does sequential delivery of CBT-I and Cognitive Processing Therapy (CPT) improve PTSD & depression, compared to CPT alone ?
3. Does sequential treatment enhance response rates achieved by CPT alone ?

3: CBT-I improves more than sleep: (b) PTSD/MDD

Recruitment: Family Court & DV Shelter

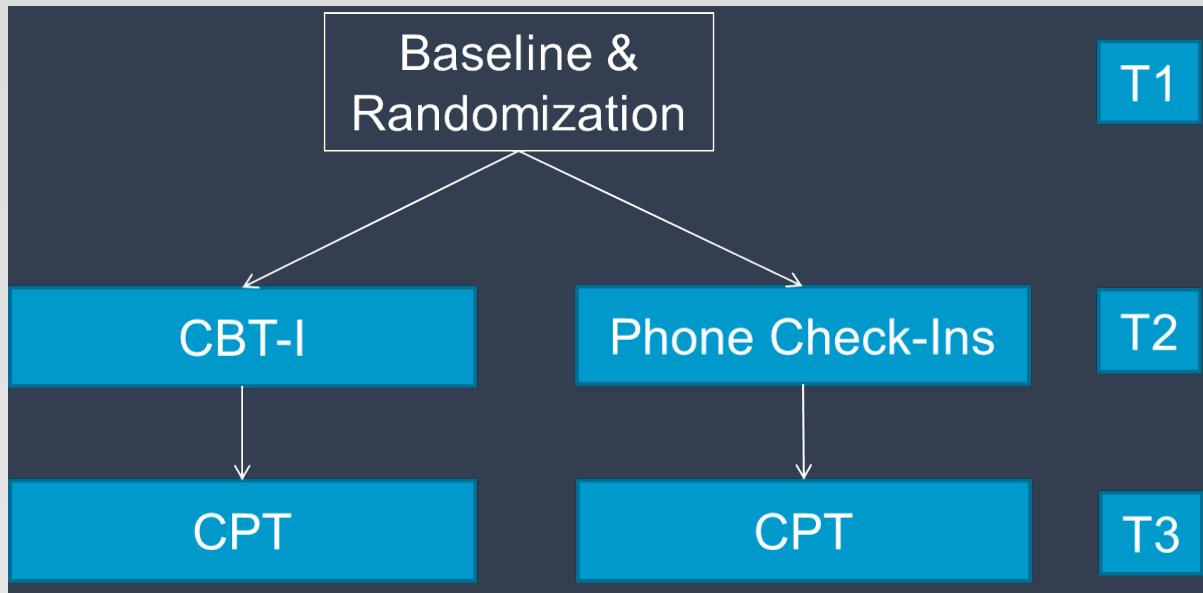


Screened Sample	% or M(SD)
Insomnia	18.6 (6.0)
Absent (0-7)	5%
Mild (8-14)	17%
Moderate (15-21)	43%
Severe (22-28)	35%
PTSD (PCL)	59.6 (14.2)
≥ 45 cutpoint	84%
Depression (PHQ)	15.7 (5.6)
None-mild (0-9)	15%
Moderate (10-14)	22%
Severe (15-24)	63%

3: CBT-I improves more than sleep: (b) PTSD/MDD

<i>Demographic Variables</i>		<i>Clinical Variables</i>	
		M (SD)	
Age	37.3 (10.8)	ISI Score	20.3 (4.1)
Hispanic/Latina	12%	HAM-D Score	24.2 (5.1)
Race		CAPS Score	75.2 (15.4)
White	49%	Fear of Sleep	36.2 (19.8)
Black/AA	38%	Suicidal Ideation	32%
Other/Multi	13%	Antidepressant Rx	17%
Income		Court Order of Protection	89%
Under \$20,000	63%	# Traumatic Life Events	5.2 (2.4)
20,000-60,000	28%		
60,001+	9%		
Education			
< High School	15%		
High School	15%		
Some College	44%		
Bachelors+	26%		

3: CBT-I improves more than sleep: (b) PTSD/MDD



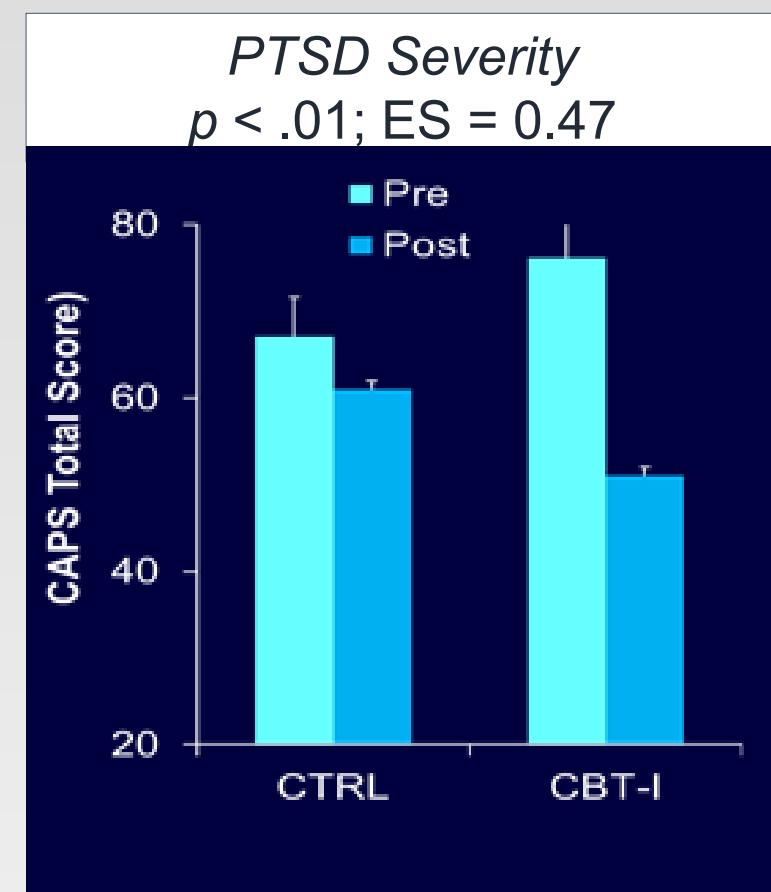
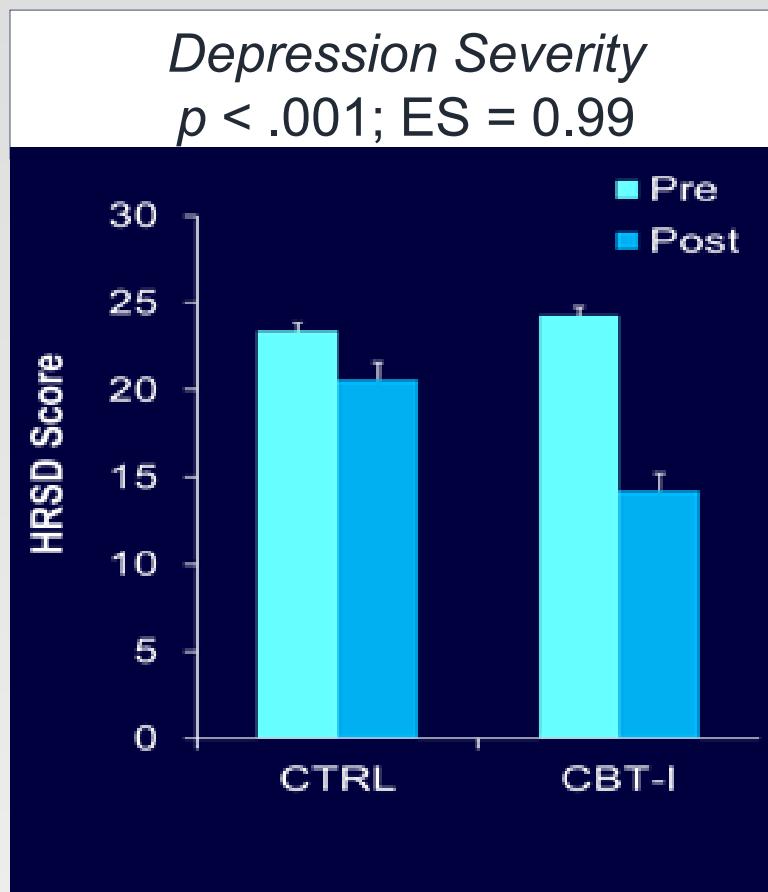
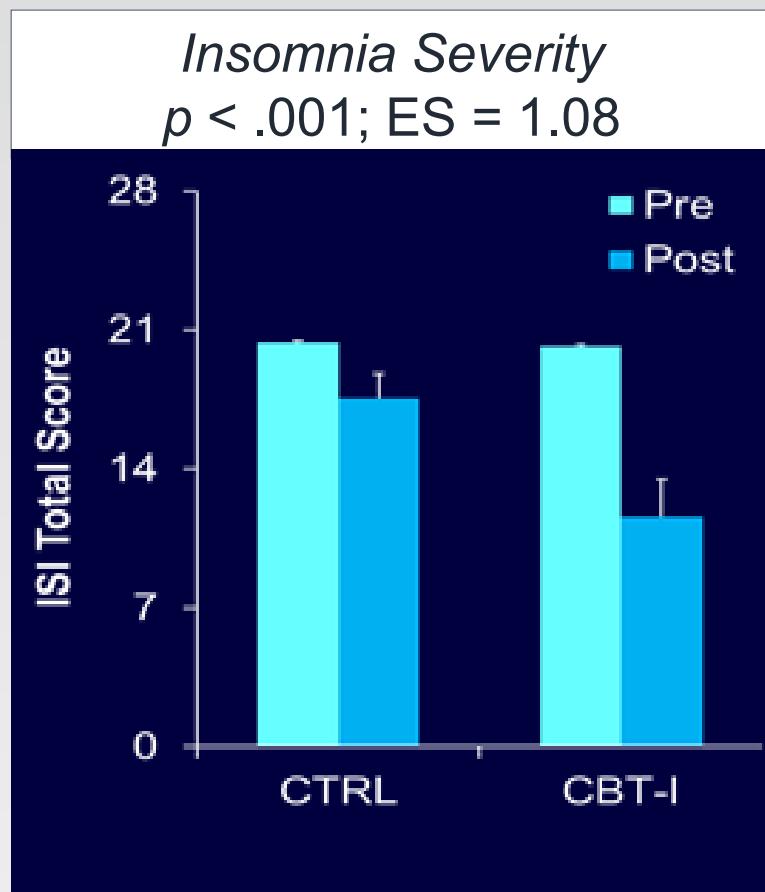
Interventions

- CBT-I:
 - Four (4) Individual Sessions over 5 weeks
- CPT:
 - Twelve (12) Individual Sessions over 12-16 wks

NIH Support: R01 NR013909

3: CBT-I improves more than sleep: (b) PTSD/MDD

Results following CBT-I *vs.* CTRL

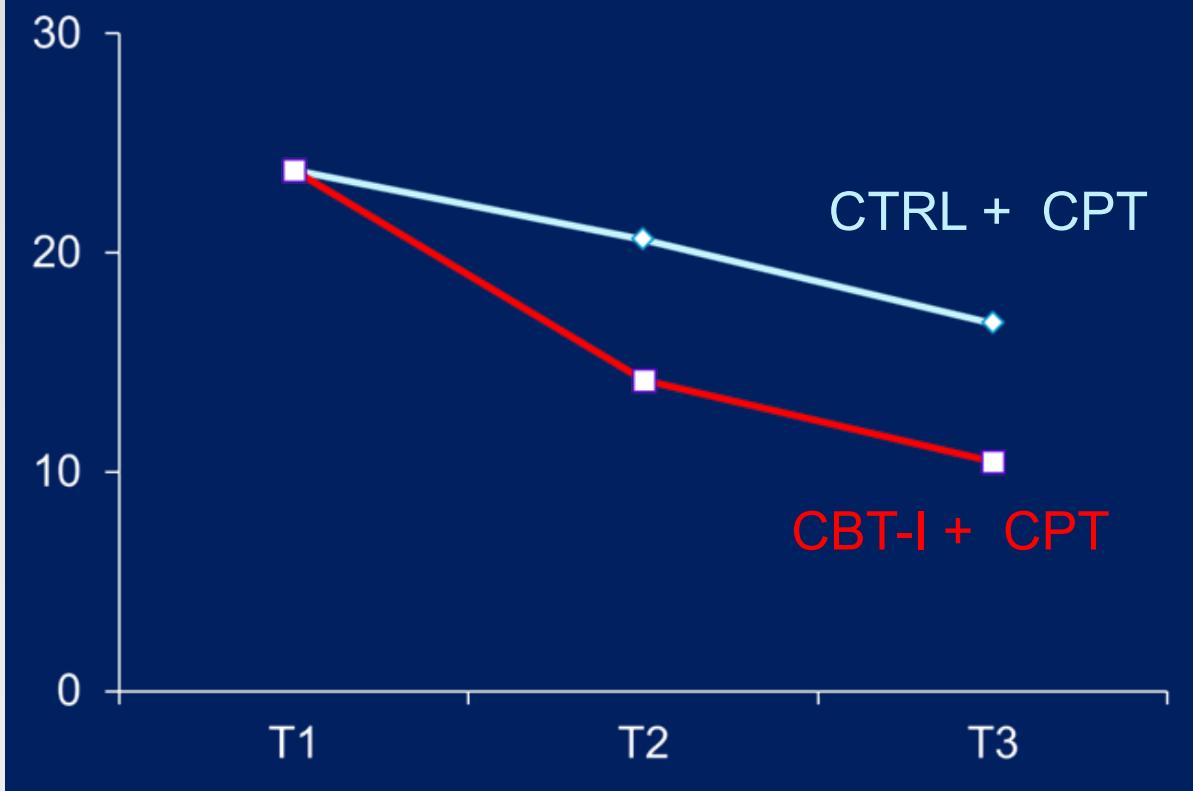


NIH Support: R01 NR013909

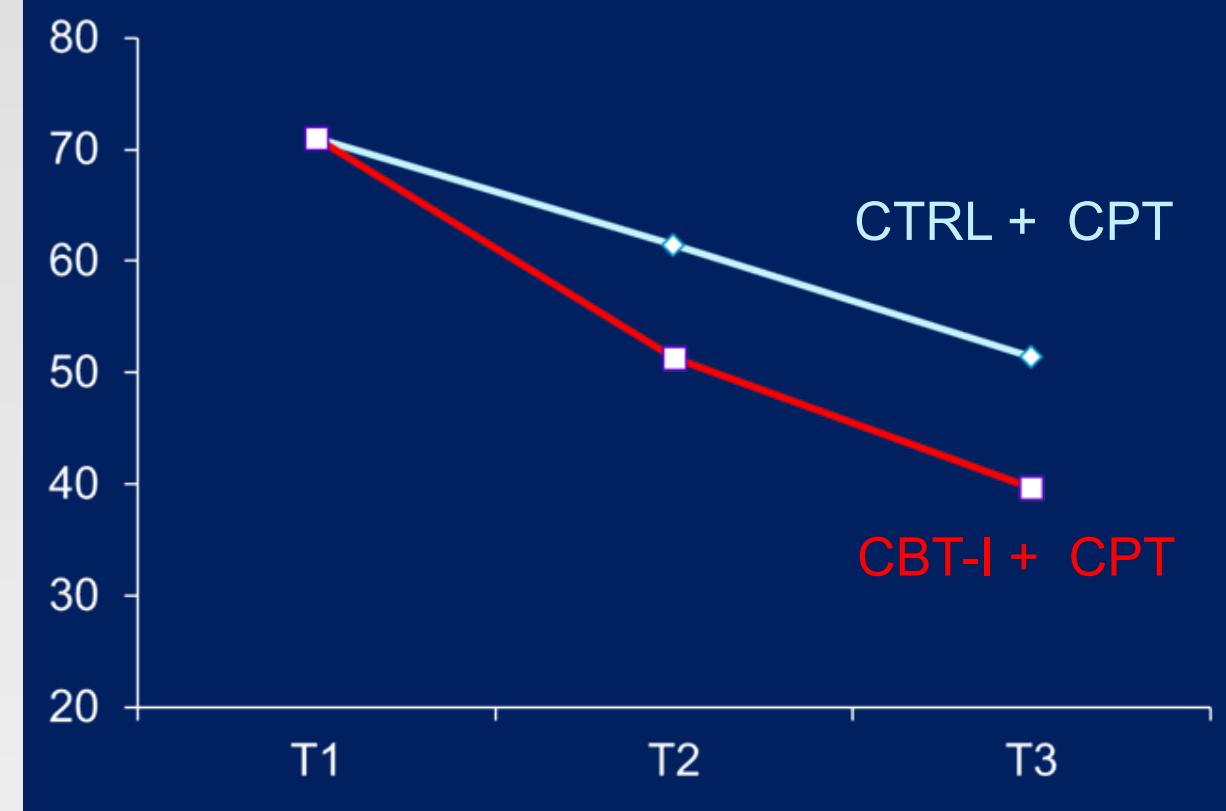
3: CBT-I improves more than sleep: (b) PTSD/MDD

Results following; CBT-I + CPT vs. CTRL + CPT

Depression (HAM-D): $p < .01$; ES = 0.82



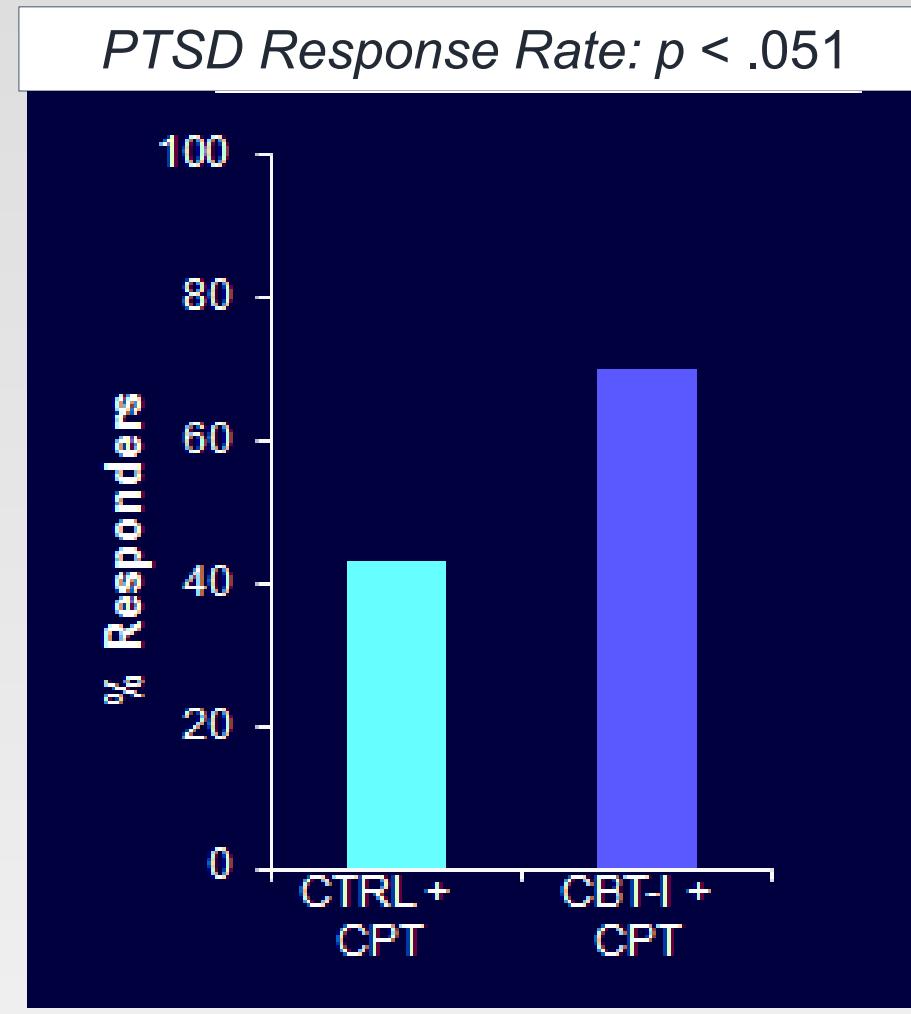
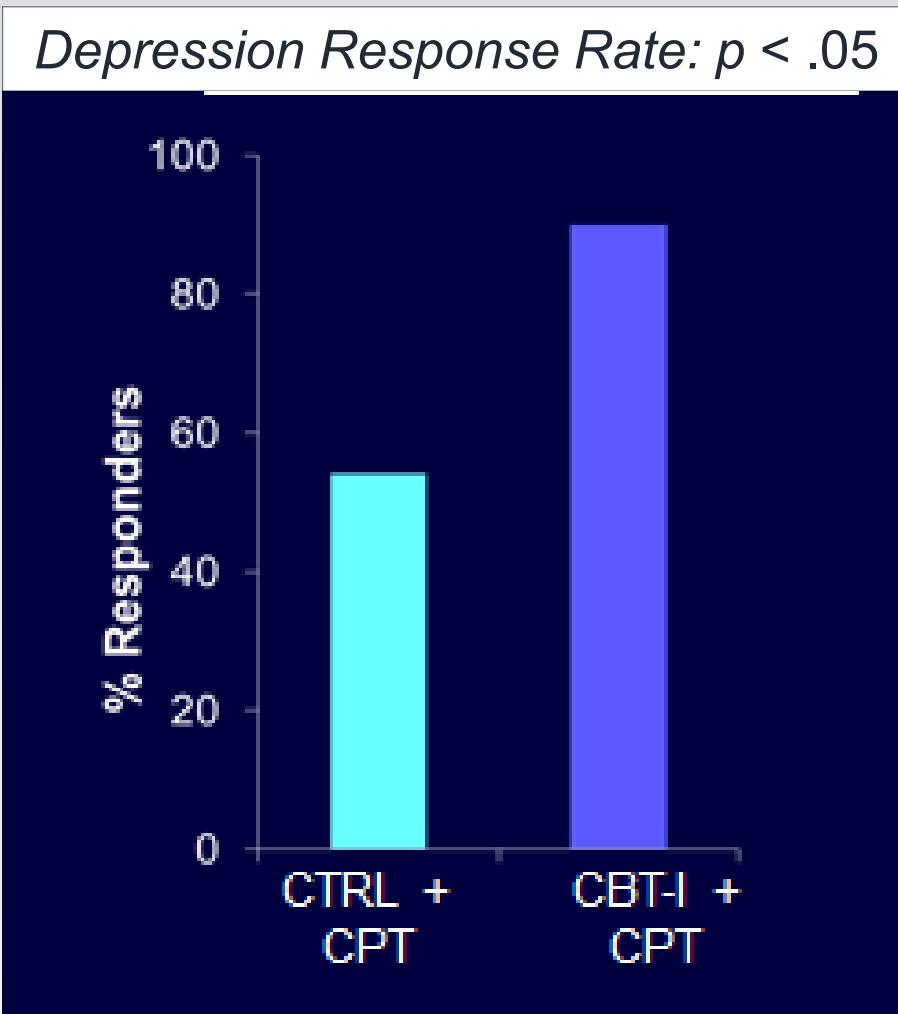
PTSD Severity (CAPS): $p = .06$; ES = 0.53



NIH Support: R01 NR013909

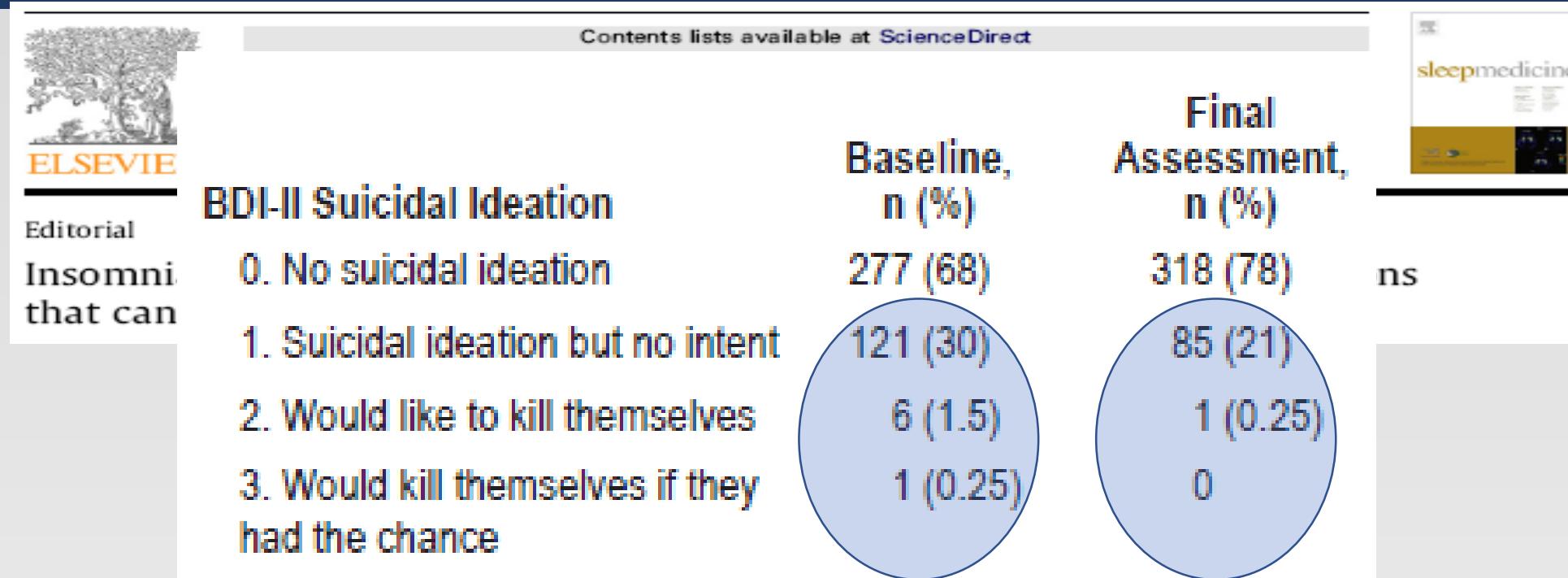
3: CBT-I improves more than sleep: (b) PTSD/MDD

Results following; CBT-I + CPT *vs.* CTRL + CPT



Premise 4: CBT-I will Reverse Climate Change

Premise 4: CBT-I = Suicide Prevention



4: CBT-I = Suicide Prevention

An RCT of *Brief* CBT-I vs. TAU in VA Primary Care

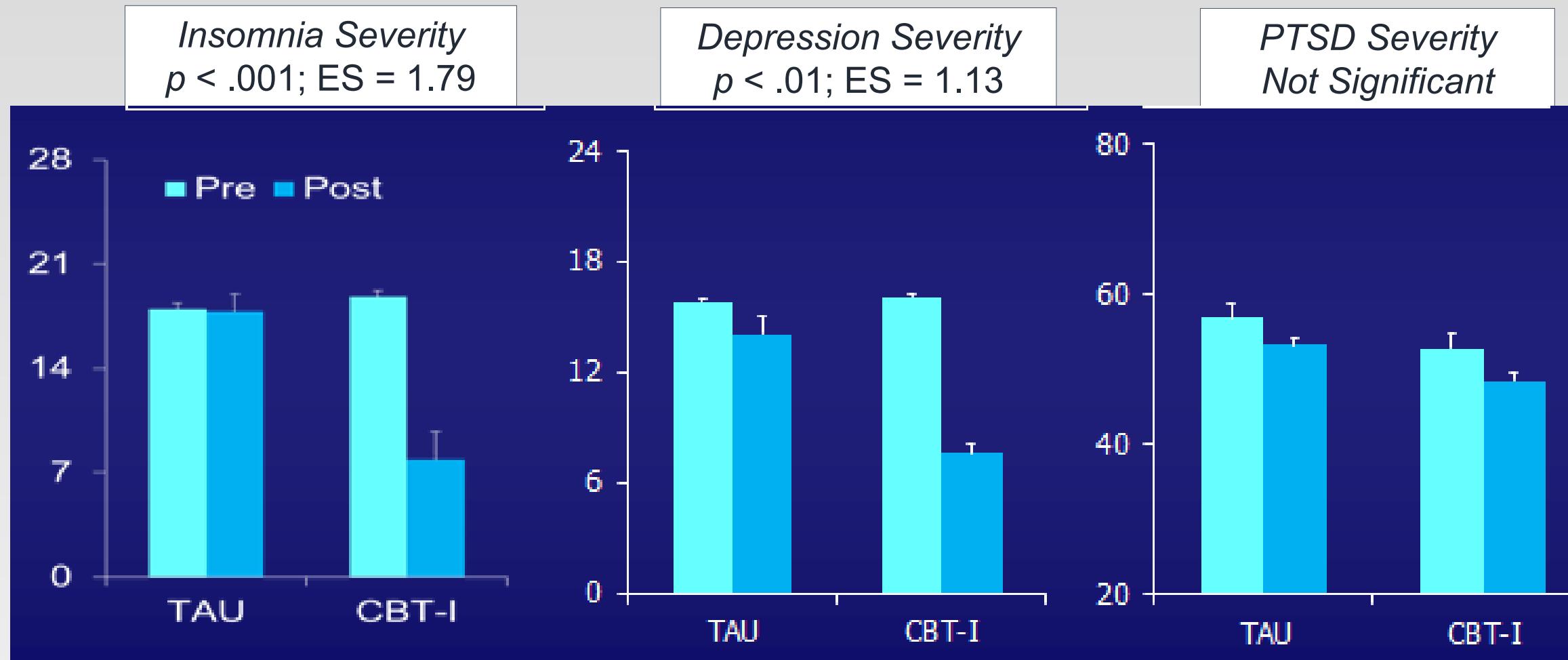
N=50 Randomized:

- Veterans in VA PC endorsing SI (without intent) + Insomnia + MDD and/or PTSD;
- identified from electronic medical record DXs
- recruited by introductory letter from their PCP
- assessed and treated in a co-located PC office
- progress notes co-signed by PCP

Brief = Two 30-40 min. sessions +
Two 15-20 min. phone sessions

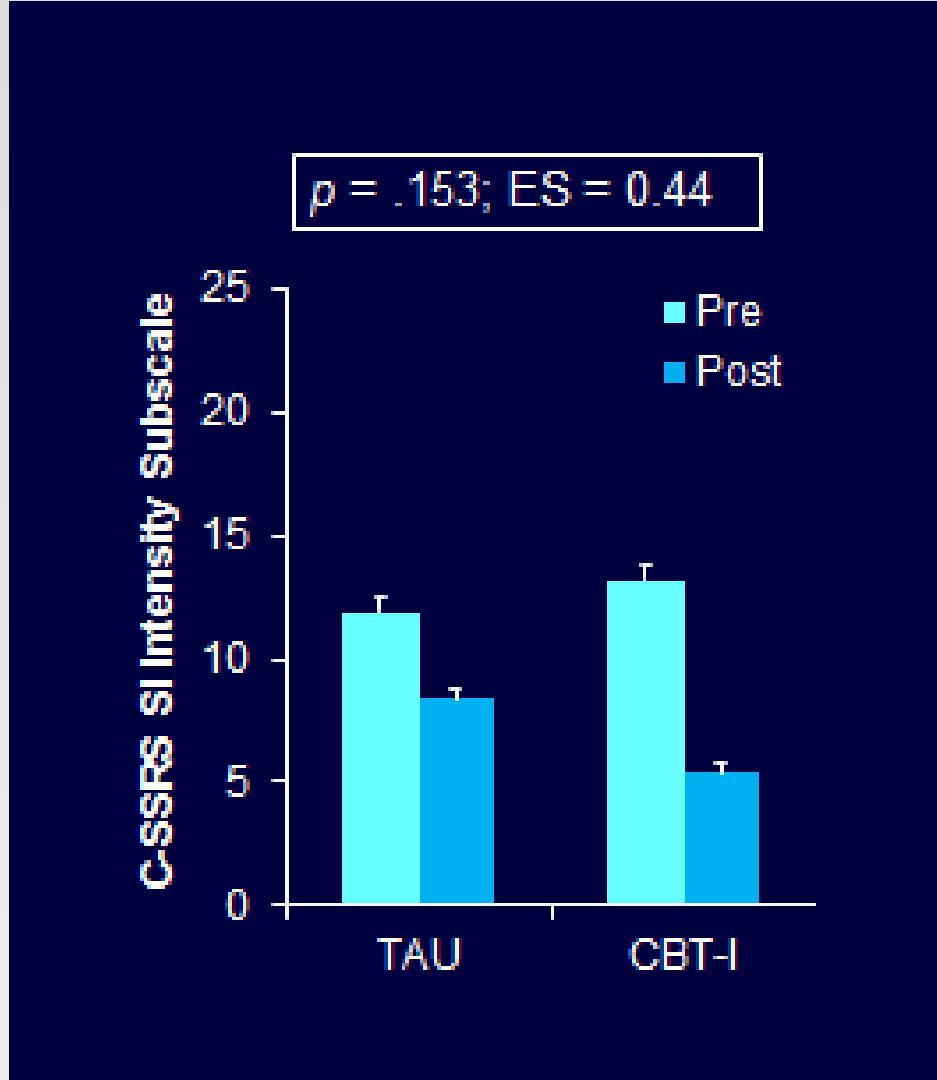
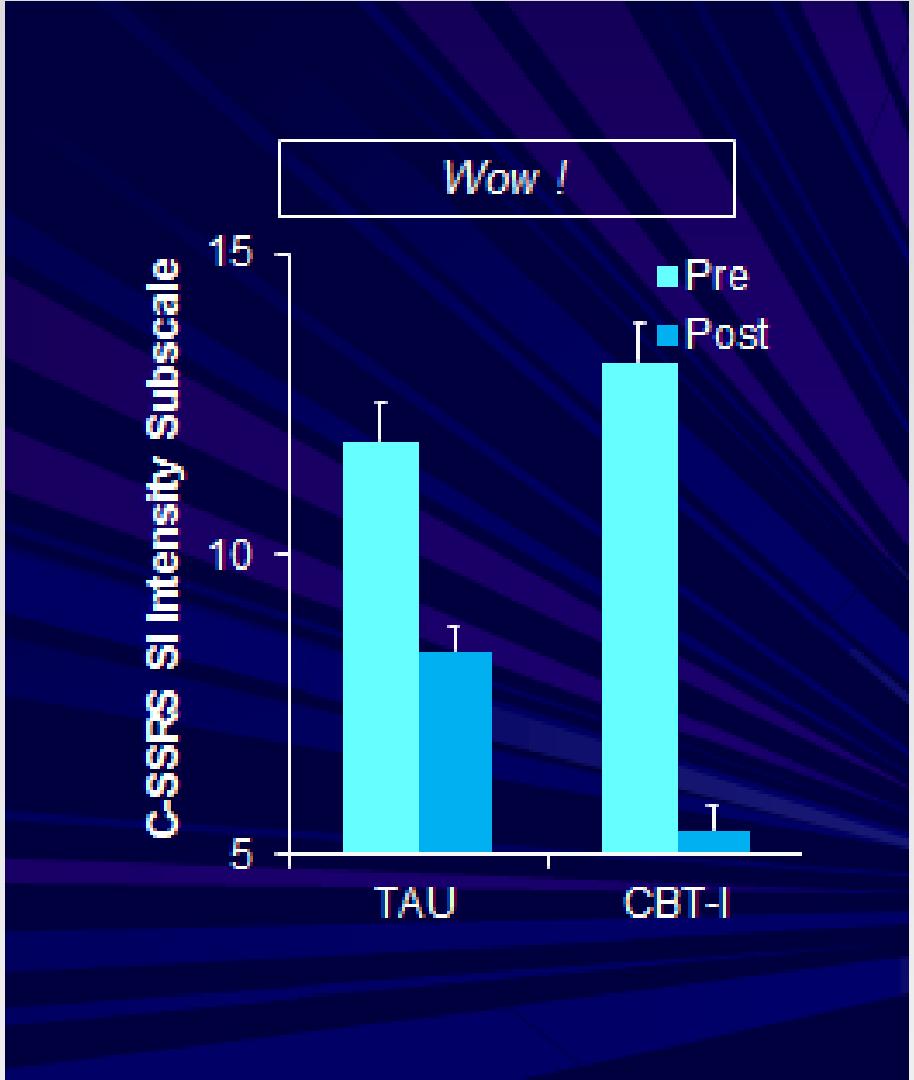
- Insomnia Severity Index (ISI)
- Patient Health Questionnaire (PHQ-9)
- PTSD SX Checklist-Military Version (PCL-M)
- Columbia-Suicide Severity Rating Scale (C-SSRS)
 - Suicidal Ideation (0-5 categorical scale)
 - Intensity of Ideation (5 items, 1-25 continuous scale)
 - Suicidal Behaviors

CBT-I vs. Treatment-as-Usual: N=50 Veterans w/ Suicidal Thoughts

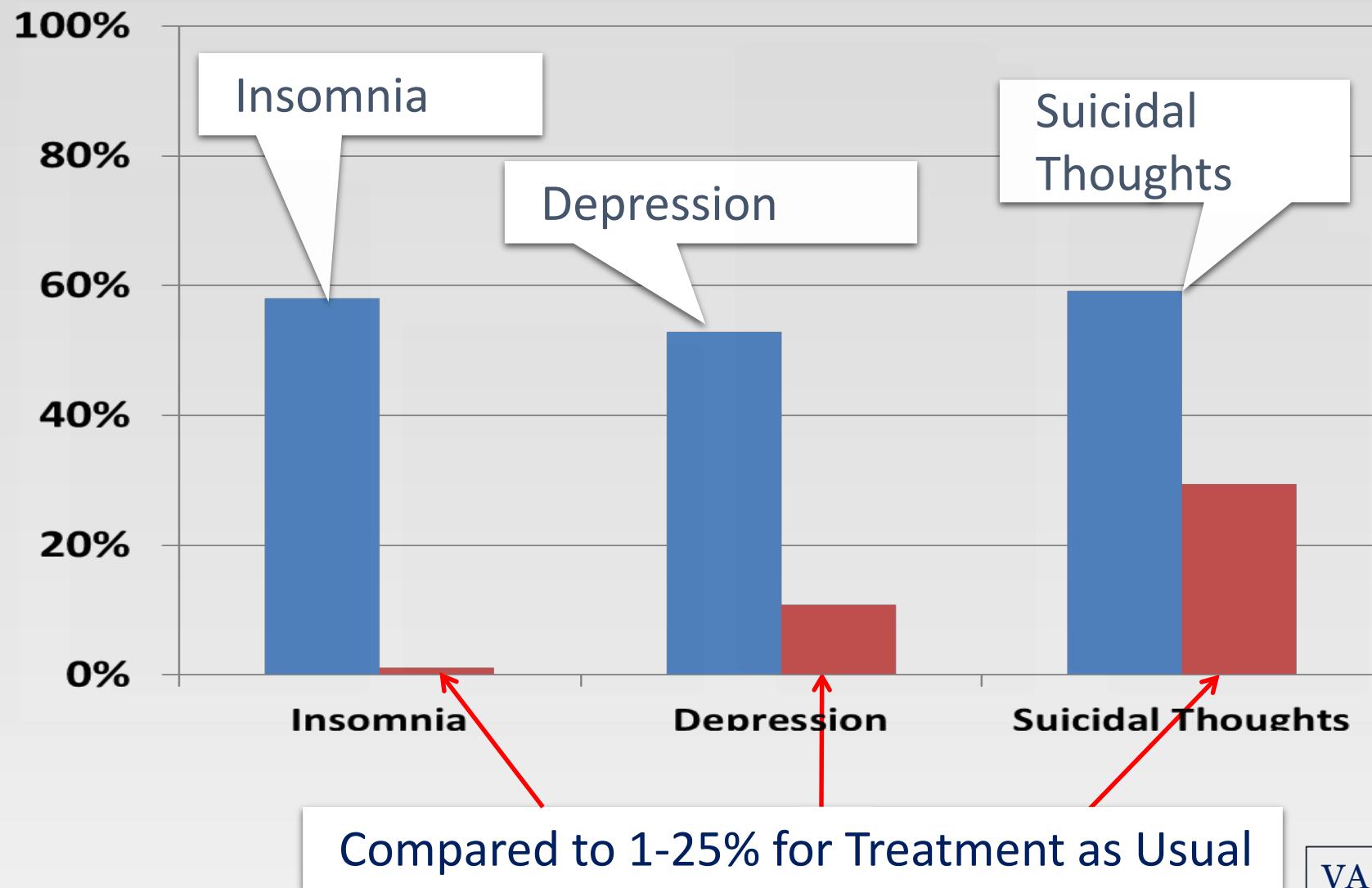


VA Support: I21 HX001616

4: CBT-I = Suicide Prevention ?



Brief CBT-I delivered in primary care reduced Sx severity by 50-60% for:

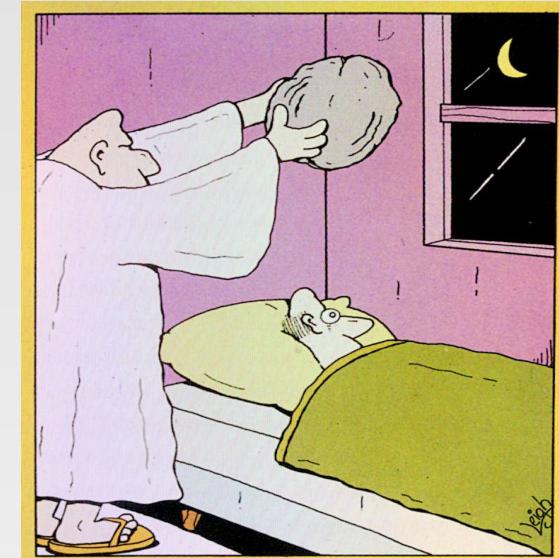


Summary

1. Sleep Disturbance (*e.g., insomnia*) exacerbates and causes medical and psychiatric morbidity
2. The efficacy, effectiveness and limited AE profile of CBT-I ‘should’ make Rx of hypnotics rare
3. Treating insomnia improves more than sleep
4. CBT-I is an anti-depressant with suicide preventing side effects

“The best bridge between despair and hope is a good night's sleep.”

-- E. Joseph Cossman

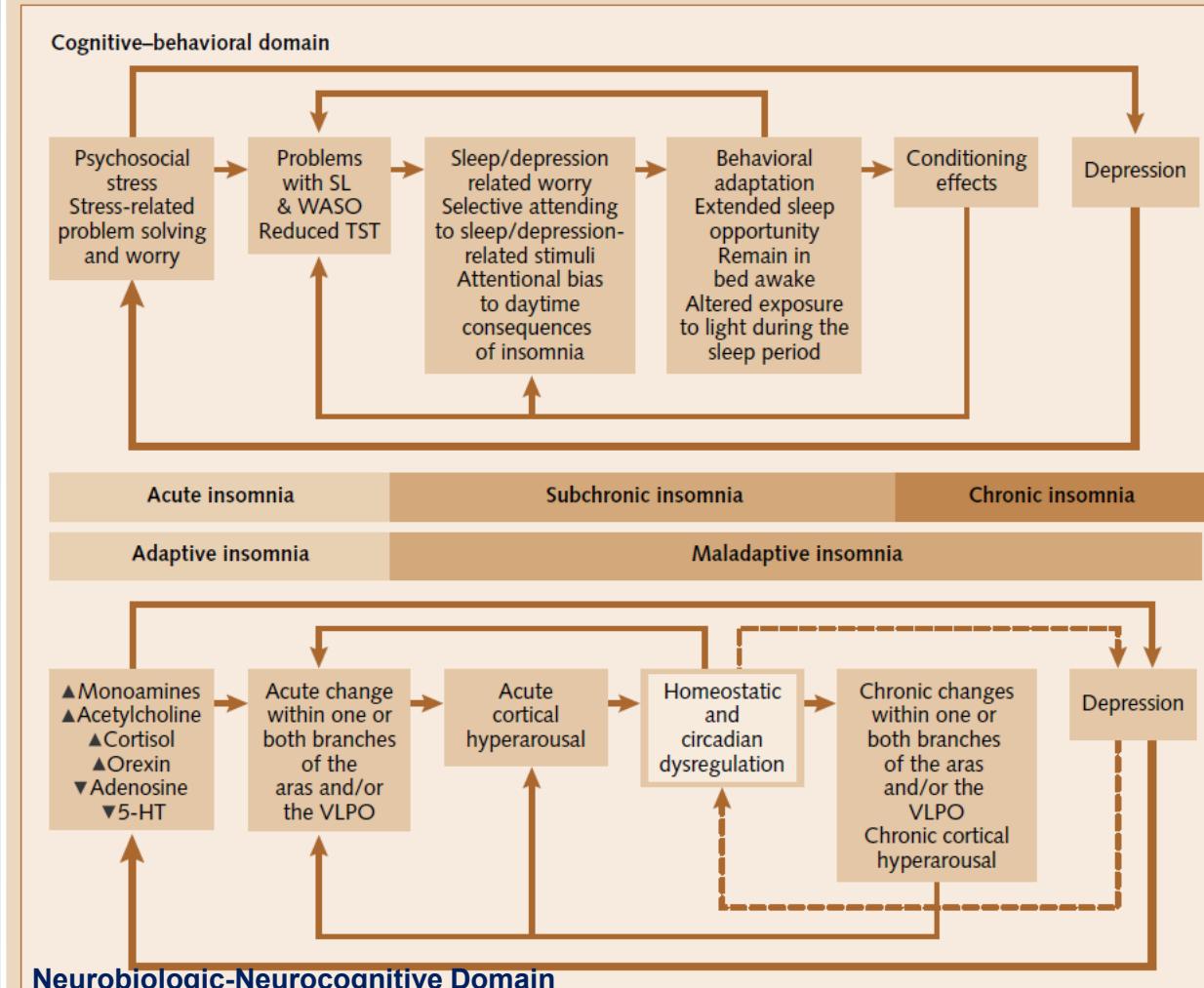


Thank You.... Closing Thoughts/Discussion



Insomnia & Depression: A parallel process model

Figure 3. Etiology and pathophysiology of insomnia and depression. The box delineating the homeostatic and circadian factors is highlighted because the neurobiological control mechanisms are not detailed.



Future Directions

- **Bishop Apnea**
- **Adolescents – C. Glenn**
- **Stecker---**
- **Combined/sequential Tx's**
- **Sleep as a ‘Mechanism’ in Cancer**
- **Sleep as a mechanism in early dementia**

Sleep Drives Metabolite Clearance from the Adult Brain

Lulu Xie,^{1*} Hongyi Kang,^{1*} Qiwu Xu,¹ Michael J. Chen,¹ Yonghong Liao,¹ Thiagarajan Meenakshisundaram,¹ John O'Donnell,¹ Daniel J. Christensen,¹ Charles Nicholson,² Jeffrey J. Iliff,¹ Takahiro Takano,¹ Rashid Deane,¹ Maiken Nedergaard^{1†}



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FOR PROVIDERS WHO TREAT VETERANS

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questions in the Q&A box
and be sure to include your
email address.

The lines are muted to avoid background noise.



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Registration → Attendance → Evaluation → Certificate



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*Listen to the
lecture.*

*Return to
TRAIN for
evaluation.*

*Follow the
directions to
print
certificate.*

TRAIN help desk: VHATRAIN@va.gov

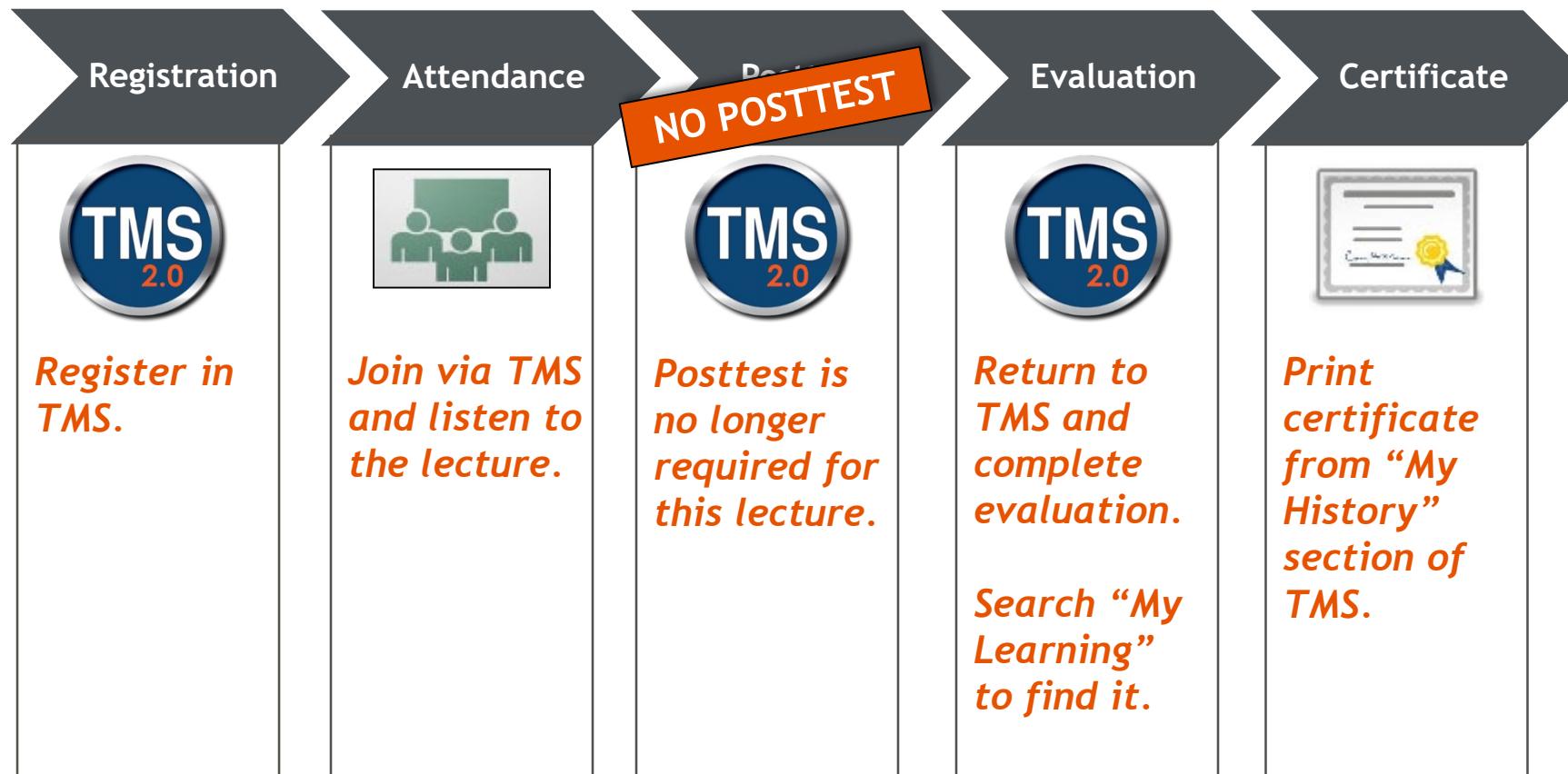


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CEU Process (for VA employees)





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UPCOMING TOPICS

SAVE THE DATE: Third Wednesday of the Month from 2-3PM (ET)

December 18 *Treating Comorbid PTSD and Borderline Personality Disorder* Melanie Harned, PhD, ABPP

January 15 *Dissociation, Somatization, and Other Challenging Presentations of PTSD* Abigail Angkaw, PhD

February 19 *Concurrent Treatment of PTSD and SUDs using Prolonged Exposure (COPE)* Sudie Back, PhD

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